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CORRECTED VERSION

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date 29 November 2001 (29.11.2001)

PCT

(10) International Publication Number WO 01/090197 A1

- (51) International Patent Classification7: C07K 19/00, C12Q 1/68, C07K 2/00, 14/005, 14/15, 14/20, 14/435, C12N 15/09
- (21) International Application Number: PCT/AU01/00622
- (22) International Filing Date: 25 May 2001 (25.05.2001)
- (25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: PQ 7761

26 May 2000 (26.05.2000) AU

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- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,

CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
 - with sequence listing part of description published separately in electronic form and available upon request from the International Bureau
- (48) Date of publication of this corrected version:

12 September 2003

(15) Information about Correction:

see PCT Gazette No. 37/2003 of 12 September 2003, Section II

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: SYNTHETIC PEPTIDES AND USES THEREFORE

(57) Abstract: A synthetic polypeptide is disclosed, which comprises a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide. Synthetic polynucleotides are also disclosed that code for the synthetic polypeptides of the invention as well as expression constructs comprising the synthetic polynucleotides. Also disclosed are methods for constructing the aforementioned molecules and immunopotentiating compositions and methods for treating and/or preventing a disease or condition.



SYNTHETIC PEPTIDES AND USES THEREFORE

FIELD OF THE INVENTION

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THIS INVENTION relates generally to agents for modulating immune responses. More particularly, the present invention relates to a synthetic polypeptide comprising a plurality of different segments of a parent polypeptide, wherein the segments are linked to each other such that one or more functions of the parent polypeptide are impeded, abrogated or otherwise altered and such that the synthetic polypeptide, when introduced into a suitable host, can elicit an immune response against the parent polypeptide. The invention also relates to synthetic polynucleotides encoding the synthetic polypeptides and to synthetic constructs comprising these polynucleotides. The invention further relates to the use of the polypeptides and polynucleotides of the invention in compositions for modulating immune responses. The invention also extends to methods of using such compositions for prophylactic and/or therapeutic purposes.

Bibliographic details of various publications referred to in this specification are collected at the end of the description.

BACKGROUND OF THE INVENTION

The modern reductionist approach to vaccine and therapy development has been pursued for a number of decades and attempts to focus only on those parts of pathogens or of cancer proteins which are relevant to the immune system. To date the performance of this approach has been relatively poor considering the vigorous research carried out and the number of effective vaccines and therapies that it has produced. This approach is still being actively pursued, however, despite its poor performance because vaccines developed using this approach are often extremely safe and because only by completely understanding the immune system can new vaccine strategies be developed.

One area that has benefited greatly from research efforts is knowledge about how the adaptive immune system operates and more specifically how T and B cells learn to recognise specific parts of pathogens and cancers. T cells are mainly involved in cell-mediated immunity whereas B cells are involved in the generation of antibody-mediated immunity. The two most important types of T cells involved in adaptive cellular immunity

are αβ CD8⁺ cytotoxic T lymphocytes (CTL) and CD4⁺ T helper lymphocytes. CTL are important mediators of cellular immunity against many viruses, tumours, some bacteria and some parasites because they are able to kill infected cells directly and secrete various factors which can have powerful effects on the spread of infectious organisms. CTLs recognise epitopes derived from foreign intracellular proteins, which are 8-10 amino acids long and which are presented by class I major histocompatibility complex (MHC) molecules (in humans called human lymphocyte antigens - HLAs) (Jardetzky et al., 1991; Fremont et al., 1992; Rotzschke et al., 1990). T helper cells enhance and regulate CTL responses and are necessary for the establishment of long-lived memory CTL. They also inhibit infectious organisms by secreting cytokines such as IFN-y. T helper cells recognise epitopes derived mostly from extracellular proteins which are 12-25 amino acids long and which are presented by class II MHC molecules (Chicz et al., 1993; Newcomb et al., 1993). B cells, or more specifically the antibodies they secrete, are important mediators in the control and clearance of mostly extracellular organisms. Antibodies recognise mainly conformational determinants on the surface of organisms, for example, although sometimes they may recognise short linear determinants.

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Despite significant advances towards understanding how T and linear B cell epitopes are processed and presented to the immune system, the full potential of epitopebased vaccines has not been fully exploited. The main reason for this is the large number of different T cell epitopes, which have to be included into such vaccines to cover the extreme HLA polymorphism in the human population. The human HLA diversity is one of the main reasons why whole pathogen vaccines frequently provide better population coverage than subunit or peptide-based vaccine strategies. There is a range of epitopebased strategies though which have tried to solve this problem, e.g., peptide blends, peptide conjugates and polyepitope vaccines (ie comprising strings of multiple epitopes) (Dyall et al., 1995; Thomson et al., 1996; Thomson et al., 1998; Thomson et al., 1998). These approaches however will always be sub optimal not only because of the slow pace of epitope characterisation but also, because it is virtually impossible for them to cover every existing HLA polymorphism in the population. A number of strategies have sought to avoid both problems by not identifying epitopes and instead incorporating larger amounts of sequence information e.g., approaches using whole genes or proteins and approaches that mix multiple protein or gene sequences together. The proteins used by these strategies

however sometimes still function and therefore can compromise vaccine safety e.g., whole cancer proteins. Alternative strategies have tried to improve the safety of vaccines by fragmenting the genes and expressing them either separately or as complex mixtures e.g., library DNA immunisation or by ligating such fragments back together. These approaches are still sub-optimal because they are too complex, generate poor levels of immunity, cannot guarantee that all proteins no longer function and/or that all fragments are present, which compromises substantially complete immunological coverage.

The lack of a safe and efficient vaccine strategy that can provide substantially complete immunological coverage is an important problem, especially when trying to develop vaccines against rapidly mutating and persistent viruses such as HIV and hepatitis C virus, because partial population coverage could allow vaccine-resistant pathogens to reemerge in the future. Human immunodeficiency virus (HIV) is an RNA lentivirus virus approximately 9 kb in length, which infects CD4⁺ T cells, causing T cell decline and AIDS typically 3-8 years after infection. It is currently the most serious human viral infection. 15 evidenced by the number of people currently infected with HIV or who have died from AIDS, estimated by the World Health Organisation (WHO) and UNAIDS in their AIDS epidemic update (December 1999) to be 33.6 and 16.3 million people, respectively. The spread of HIV is also now increasing fastest in areas of the world where over half of the human population reside, hence an effective vaccine is desperately needed to curb the 20 spread of this epidemic. Despite the urgency, an effective vaccine for HIV is still some way off because of delays in defining the correlates of immune protection, lack of a suitable animal model, existence of up to 8 different subtypes of HIV and a high HIV mutation rate.

A significant amount of research has been carried out to try and develop a vaccine capable of generating neutralising antibody responses that can protect against field isolates of HIV. Despite these efforts, it is now clear that the variability, instability and inaccessibility of critical determinants on the HIV envelope protein will make it extremely difficult and perhaps impossible to develop such a vaccine (Kwong et al., 1998). The limited ability of antibodies to block HIV infection is also supported by the observation that development of AIDS correlates primarily with a reduction in CTL responsiveness to HIV and not to altered antibody levels (Ogg et al., 1998). Hence CTL-mediated and not antibody-mediated responses appear to be critical for maintaining the asymptomatic state

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in vivo. There is also some evidence to suggest that pre-existing HIV-specific CTL responses can block the establishment of a latent HIV infection. This evidence comes from a number of cases where individuals have generated HIV-specific CTL responses without becoming infected and appear to be protected from establishing latent HIV infections despite repeated virus exposure (Rowland-Jones et al., 1995; Parmiani 1998). Taken together, these observations suggest that a vaccine capable of generating a broad range of strong CTL responses may be able to stop individuals from becoming latently infected with HIV or at least allow infected individuals to remain asymptomatic for life. Virtually all of the candidate HIV vaccines developed to date have been derived from subtype B HTV proteins (western world subtype) whereas the majority of the HIV infections worldwide are caused by subtypes A/E or C (E and A are similar except in the envelop protein)(referred to as developing world subtypes). Hence existing candidate vaccines may not be suitable for the more common HIV subtypes. Recently, there has been some evidence that B subtype vaccines may be partially effective against other common HIV subtypes (Rowland-Jones et al., 1998). Accordingly, the desirability of a vaccine still remains, whose effectiveness is substantially complete against all isolates of all strains of HIV.

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SUMMARY OF THE INVENTION

The present invention is predicated in part on a novel strategy for enhancing the efficacy of an immunopotentiating composition. This strategy involves utilising the sequence information of a parent polypeptide to produce a synthetic polypeptide that 5 comprises a plurality of different segments of the parent polypeptide, which are linked sequentially together in a different arrangement relative to that of the parent polypeptide. As a result of this change in relationship, the sequence of the linked segments in the synthetic polypeptide is different to a sequence contained within the parent polypeptide. As more fully described hereinafter, the present strategy is used advantageously to cause significant disruption to the structure and/or function of the parent polypeptide while minimising the destruction of potentially useful epitopes encoded by the parent polypeptide.

Thus, in one aspect of the present invention, there is provided a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, 15 wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

In one embodiment, the synthetic polypeptide consists essentially of different segments of a single parent polypeptide.

In an alternate embodiment, the synthetic polypeptide consists essentially of 20 different segments of a plurality of different parent polypeptides.

Suitably, said segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to that of corresponding segments in said at least one parent polypeptide.

Preferably, at least one of said segments comprises partial sequence identity or homology to one or more other said segments. The sequence identity or homology is 25 preferably contained at one or both ends of said at least one segment.

In another aspect, the invention resides in a synthetic polynucleotide encoding the synthetic polypeptide as broadly described above.

According to yet another aspect, the invention contemplates a synthetic construct comprising a said polynucleotide as broadly described above that is operably linked to a regulatory polynucleotide.

In a further aspect of the invention, there is provided a method for producing a synthetic polynucleotide as broadly described above, comprising:

- linking together in the same reading frame a plurality of nucleic acid sequences encoding different segments of at least one parent polypeptide to form a synthetic polynucleotide whose sequence encodes said segments linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

Preferably, the method further comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking said fragments together in a different relationship relative to their linkage in said parent polypeptide sequence. In a preferred embodiment of this type, the fragments are randomly linked together.

Suitably, the method further comprises reverse translating the sequence of a respective parent polypeptide or a segment thereof to provide a nucleic acid sequence encoding said parent polypeptide or said segment. In a preferred embodiment of this type, an amino acid of said parent polypeptide sequence is reverse translated to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest. Suitably, an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence (e.g., a palindromic sequence or a duplicated sequence) that is refractory to the execution of a task (e.g., cloning or sequencing).

In another aspect, the invention encompasses a computer program product for designing the sequence of a synthetic polypeptide as broadly described above, comprising:

- code that receives as input the sequence of at least one parent polypeptide;
- code that fragments the sequence of a respective parent polypeptide into fragments;

- code that links together said fragments in a different relationship relative to their linkage in said parent polypeptide sequence; and
 - a computer readable medium that stores the codes.

In yet another aspect, the invention provides a computer program product for designing the sequence of a synthetic polynucleotide as broadly described above, comprising:

- code that receives as input the sequence of at least one parent polypeptide;
- code that fragments the sequence of a respective parent polypeptide into fragments:
- 10 - code that reverse translates the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment;
 - code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence; and
 - a computer readable medium that stores the codes.

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In still yet another aspect, the invention provides a computer for designing the sequence of a synthetic polypeptide as broadly described above, wherein said computer comprises:

- 20 (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
 - (b) a working memory for storing instructions for processing said machine-readable data;
- 25 (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polypeptide sequence; and
 - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence.

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In a preferred embodiment, the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking together said fragments in a different relationship relative to their linkage in the sequence of said parent polypeptide.

In still yet another aspect, the invention resides in a computer for designing the sequence of a synthetic polynucleotide as broadly described above, wherein said computer comprises:

- (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
- (b) a working memory for storing instructions for processing said machine-readable data;
- (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polynucleotide sequence; and
- (d) an output hardware coupled to said central processing unit, for receiving said synthetic polynucleotide sequence.

In a preferred embodiment, the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments, reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment and linking together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence.

According to another aspect, the invention contemplates a composition, comprising an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polynucleotide as broadly described above and a synthetic construct as broadly described above, together with a pharmaceutically acceptable carrier.

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The composition may optionally comprise an adjuvant.

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In a further aspect, the invention encompasses a method for modulating an immune response, which response is preferably directed against a pathogen or a cancer, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polynucleotide as broadly described above and a synthetic construct as broadly described above, or a composition as broadly described above.

According to still a further aspect of the invention, there is provided a method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polynucleotide as broadly described above and a synthetic construct as broadly described above, or a composition as broadly described above.

The invention also encompasses the use of the synthetic polypeptide, the synthetic polynucleotide and the synthetic construct as broadly described above in the study, and modulation of immune responses.

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BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a diagrammatic representation showing the number of people living with AIDS in 1998 in various parts of the world and most prevalent HIV clades in these regions. Estimates generated by UNAIDS.

Figure 2 is a graphical representation showing trends in the incidence of the common HIV clades and estimates for the future. Graph from the International Aids Vaccine Initiative (IAVI).

Figure 3 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV gag [SEQ ID NO: 1] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV gag protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 4 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV pol [SEQ ID NO: 2] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV pol protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR98-485.

Figure 5 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vif [SEQ ID NO: 3] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV vif protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR98-485.

Figure 6 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vpr [SEQ ID NO: 4] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV vpr protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 7 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV tat [SEQ ID NO: 5] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV tat protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 8 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV rev [SEQ ID NO: 6] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV rev protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

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Figure 9 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vpu [SEQ ID NO: 7] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV vpu protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 10 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV env [SEQ ID NO: 8] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade

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consensus sequences for the HIV env protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 11 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV nef [SEQ ID NO: 9] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV nef protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 12 is a diagrammatic representation depicting the systematic segmentation of the designed degenerate consensus sequences for each HIV protein and the reverse translation of each segment into a DNA sequence. Also shown is the number of segments used during random rearrangement and amino acids that were removed. Amino acids surrounded by an open square were removed from the design, because degenerate codons to cater for the desired amino acid combination required too many degenerate bases to comply with the incorporation of degenerate sequence rules outlined in the description of the invention herein. Amino acids surrounded by an open circle were removed only in the segment concerned mainly because they were coded for in an oligonucleotide overlap region. Amino acids marked with an asterisk were designed differently in one fragment compared to the corresponding overlap region (see tat gene)

Figure 13 is a diagrammatic representation showing the first and second most frequently used codons in mammals used to reverse translate HIV protein segments. Also shown are all first and second most frequently used degenerate codons for two amino acids where only one base is varied. Codons used where more than one base was varied were worked out in each case by comparing all the codons for each amino acid. The IUPAC codes for degenerate bases are also shown.

Figure 14 illustrates the construction plan for the HIV Savine showing the approximate sizes of the subcassettes, cassettes and full-length Savine cDNA and the restriction sites involved in joining them together. Also shown are the extra sequences

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added onto each subcassette during their design and a brief description of how the subcassettes, cassettes and full length cDNA were constructed and transferred into appropriate DNA plasmids. Description of full length construction: pA was cleaved with XhoI/SalI and cloned into XhoI arms of the B cassette; pAB was cleaved with XhoI and cloned into XhoI arms of the C cassette; full length construct is excisable with either XbaI/BamHI at the 5' end or BglII at the 3' end. Options for excising cassettes: A) XbaI/BamHI at the 5' end, BglII/XhoI at the 3' end; B) XbaI/BamHI at the 5' end, BglII/SalI at the 3' end; C) XbaI/BamHI at the 5' end, BglII/SalI at the 3' end. Cleaving plasmid vectors: pDNAVacc is cleavable with XbaI/XhoI (DNA vaccination); pBCB07 or pTK7.5 vectors are cleavable with BamHI/SalI (Recombinant Vaccinia); pAvipox vector pAF09 is cleavable with BamHI/SalI (Recombinant Avipox).

Figure 15 shows the full length DNA (17253 bp) and protein sequence (5742 aas) of the HIV Savine construct. Fragment boundaries are shown, together with the position of each fragment in each designed HIV protein, fragment number (in brackets), spacer residues (two alanine residues) and which fragment the spacer was for (open boxes and arrows). The location of residual restriction site joining sequences corresponding to subcassette or cassette boundaries (shaded boxes) are also shown, along with start and stop codons, Kozak sequence, the location of the murine influenza virus CTL epitope sequence (near the 3' end), important restriction sites at each end and the position of each degenerate amino acid (indicated by 'X').

Figure 16 depicts the layout and position of oligonucleotides in the designed DNA sequence for subcassette A1. The sequences which anneal to the short amplification oligonucleotides are indicated by hatched boxes and the position of oligonucleotide overlap regions are dark shaded.

Figure 17: Panel (a) depicts the stepwise asymmetric PCR of the two halves of subcassette A1 (lanes 2-5 and 7-9, respectively) and final splicing together by SOEing (lane 10). DNA standards in lane 1 are pUC18 digested with Sau3AI. Panel (b) shows the stepwise ligation-mediated joining and PCR amplification of each cassette as indicated. DNA standards in lane 1 are SPP1 cut with EcoRI.

Figure 18: Panel (a) shows summary of the construction of the DNA vaccine plasmids that express one HIV Savine cassette. Panel (b) shows a summary of the

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construction of the plasmids used for marker rescue recombination to generate Vaccinia viruses expressing one HIV Savine cassette. Panel (c) shows a summary of the construction of the DNA vaccine plasmids which each express a version of the full-length HIV Savine cDNA

Figure 19 shows restimulation of HIV specific polyclonal CTL responses from three HIV-infected patients by the HIV Savine constructs. PBMCs from three different patients were restimulated for 7 days by infection with Vaccinia virus pools expressing the HIV Savine cassettes: Pool 1 included VV-AC1 and VV-BC1; Pool 2 included VV-AC2, VV-BC2 and VV-CC2. The restimulated PBMCs were then mixed with autologous LCLs (effector to target ratio of 50:1), which were either uninfected or infected with either Vaccinia viruses expressing the HIV proteins gag (VV-gag), env (VV-env) or pol (VVpol), VV- HIV Savine pools 1 (light bars) or 2 (dark bars) or a control Vaccinia virus (VV-Lac) and the amount of ⁵¹Cr released used to determine percent specific lysis. K562 cells were used to determine the level of NK cell-mediated killing in their stimulated culture.

Figure 20 is a diagrammatic representation showing CD4+ proliferation of PBMCs from HIV-1 infected patients restimulated with either Pool1 or Pool2 of the HIV-1 Savine. Briefly PBMCs were stained with CFSE and culture for 6 days with or without VVs encoding either pool1 or pool2 of the HIV-1 Savine. Restimulated Cells were then labelled with antibodies and analysed by FACS.

Figure 21 is a graphical representation showing the CTL response in mice vaccinated with the HIV Savine. C57BL6 mice were immunised with the HIV-1 Savine DNA vaccine comprising the six plasmids described in Figure 18a (100 µg total DNA was given as 50 μ g/leg i.m.). One week later Poxviruses (1x10⁷ pfu) comprising Pool 1 of the HIV-1 Savine were used to boost the immune responses. Three weeks later splenocytes 25 from these mice were restimulated with VV-Pool 1 or VV-Pool 2 for 5 days and the resultant effectors used in a 51Cr release cytotoxicity assay against targets infected with CTRVV, VV-pools or VV expressing the natural antigens from HIV-1.

Figure 22 shows immune responses of HTV Immune Macaques (vaccinated with recombinant FPV expressing gag-pol and challenged with HIV-1 2 years prior to experiment). Monkeys 1 and 2 were immunised once at day 0 with VV Savine pool 1 (Three VVs which together express the entire HIV Savine). Monkey 3 was immunised

twice with FPV-gag-pol i.e., Day 0 is 3 weeks after first FPV-gag-pol immunisation. A) IFN-y detection by ELISPOT of whole blood (0.5 mL, venous blood heparinanticoagulated) stimulated with Aldrithiol-2 inactivated whole HIV-1 (20 hours, 20 μg/mL). Plasma samples were then centrifuged (1000xg) and assayed in duplicate for antigen-specific IFN using capture ELISA. B) Flow cytometric detection of HIV-1 specific CD69+/CD8+ T cells. Freshly isolated PBMCs were stimulated with inactivated HIV-1 as above for 16 hours, washed and labelled with the antibodies. Cells were then analysed using a FACScaliburTM flow cytometer and data. analysed using Cell-Quest software. C) Flow cytometric detection of HIV-1 specific CD69+/CD4+ T cells carried out as in B).

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Figure 23 shows a diagram of a system used to carry out the instructions encoded by the storage medium of Figures 28 and 29.

Figure 24 depicts a flow diagram showing an embodiment of a method for designing synthetic polynucleotide and synthetic polypeptides of the invention.

Figure 25 shows an algorithm, which *inter alia* utilises the steps of the method shown in Figure 24.

Figure 26 shows an example of applying the algorithm of Figure 25 to an input consensus polyprotein sequence of Hepatitis C 1a to execute the segmentation of the polyprotein sequence, the rearrangement of the segments, the linkage of the rearranged segments and the outputting of synthetic polynucleotide and polypeptide sequences for the preparation of Savines for treating and/or preventing Hepatitis C infection.

Figure 27 illustrates an example of applying the algorithm of Figure 25 to input consensus melanocyte differentiation antigens (gp100, MART, TRP-1, Tyros, Trp-2, MC1R, MUC1F and MUC1R) and to consensus melanoma specific antigens (BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b and LAGE1) to facilitate segmentation of those sequences, to rearrange the segments, to link the rearranged segments and to synthetic polynucleotide and polypeptide sequences for the preparation of Savines for treating and/or preventing melanoma.

Figure 28 shows a cross section of a magnetic storage medium.

Figure 29 shows a cross section of an optically readable data storage medium.

Figure 30 shows six HIV Savine cassette sequences (A1 [SEQ ID NO: 393], A2 [SEQ ID NO: 399], B1[SEQ ID NO: 395], B2 [SEQ ID NO: 401], C1 [SEQ ID NO: 397] and C2 [SEQ ID NO: 403]). A1, B1 and C1 can be joined together using, for example, convenient restriction enzyme sites provided at the ends of each cassette to construct an embodiment of a full length HIV Savine [SEQ ID NO: 405]. A2, B2 and C2 can also be joined together to provide another embodiment of a full length HIV Savine with 350 aa mutations common in major HIV clades. The cassettes A/B/C can be joined into single constructs using specific restriction enzyme sites incorporated after the start codon or before the stop codon in the cassettes

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BRIEF DESCRIPTION OF THE SEQUENCES: SUMMARY TABLE

TABLE A

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| SIQUENCE ID NCMBER | SEÇLEVCE | LENGTH |
|-----------------------|--------------------------------------|--------|
| SEQ ID NO: 1 | GAG consensus polypeptide | 499 aa |
| SEQ ID NO: 2 | POL consensus polypeptide | 995 aa |
| SEQ ID NO: 3 | VIF consensus polypeptide | 192 aa |
| SEQ ID NO: 4 | VPR consensus polypeptide | 96 aa |
| SEQ ID NO: 5 | TAT consensus polypeptide | 102 aa |
| SEQ ID NO: 6 | REV consensus polypeptide | 123 aa |
| SEQ ID NO: 7 | VPU consensus polypeptide | 81 aa |
| SEQ ID NO: 8 | ENV consensus polypeptide | 651 aa |
| SEQ ID NO: 9 | NEF consensus polypeptide | 206 aa |
| SEQ ID NO: 10 | GAG segment 1 | 90 nts |
| SEQ ID NO: 11 | Polypeptide encoded by SEQ ID NO: 10 | 30 aa |
| SEQ ID NO: 12 | GAG segment 2 | 90 nts |
| SEQ ID NO: 13 | Polypeptide encoded by SEQ ID NO: 12 | 30 aa |
| SEQ ID NO: 14 | GAG segment 3 | 90 nts |
| SEQ ID NO: 15 | Polypeptide encoded by SEQ ID NO: 14 | 30 aa |
| SEQ ID NO: 16 | GAG segment 4 | 90 nts |
| SEQ ID NO: 17 | Polypeptide encoded by SEQ ID NO: 16 | 30 aa |
| SEQ ID NO: 18 | GAG segment 5 | 90 nts |
| SEQ ID NO: 19 | Polypeptide encoded by SEQ ID NO: 18 | 30 aa |
| SEQ ID NO: 20 | GAG segment 6 | 90 nts |
| SEQ ID NO: 21 | Polypeptide encoded by SEQ ID NO: 20 | 30 aa |
| SEQ ID NO: 22 | GAG segment 7 | 90 nts |

| SEQUENCE ID NUMBER | SIGNESCE | LENGTH |
|-----------------------|--------------------------------------|--------|
| SEQ ID NO: 23 | Polypeptide encoded by SEQ ID NO: 22 | 30 aa |
| SEQ ID NO: 24 | GAG segment 8 | 90 nts |
| SEQ ID NO: 25 | Polypeptide encoded by SEQ ID NO: 24 | 30 aa |
| SEQ ID NO: 26 | GAG segment 9 | 90 nts |
| SEQ ID NO: 27 | Polypeptide encoded by SEQ ID NO: 26 | 30 aa |
| SEQ ID NO: 28 | GAG segment 10 | 90 nts |
| SEQ ID NO: 29 | Polypeptide encoded by SEQ ID NO: 28 | 30 aa |
| SEQ ID NO: 30 | GAG segment 11 | 90 nts |
| | | |
| SEQ ID NO: 31 | Polypeptide encoded by SEQ ID NO: 30 | 30 aa |
| SEQ ID NO: 32 | GAG segment 12 | 90 nts |
| SEQ ID NO: 33 | Polypeptide encoded by SEQ ID NO: 32 | 30 aa |
| SEQ ID NO: 34 | GAG segment 13 | 90 nts |
| SEQ ID NO: 35 | Polypeptide encoded by SEQ ID NO: 34 | 30 aa |
| SEQ ID NO: 36 | GAG segment 14 | 90 nts |
| SEQ ID NO: 37 | Polypeptide encoded by SEQ ID NO: 36 | 30 aa |
| SEQ ID NO: 38 | GAG segment 15 | 90 nts |
| SEQ ID NO: 39 | Polypeptide encoded by SEQ ID NO: 38 | 30 aa |
| SEQ ID NO: 40 | GAG segment 16 | 90 nts |
| SEQ ID NO: 41 | Polypeptide encoded by SEQ ID NO: 40 | 30 aa |
| SEQ ID NO: 42 | GAG segment 17 | 90 nts |
| SEQ ID NO: 43 | Polypeptide encoded by SEQ ID NO: 42 | 30 aa |
| SEQ ID NO: 44 | GAG segment 18 | 90 nts |
| SEQ ID NO: 45 | Polypeptide encoded by SEQ ID NO: 44 | 30 aa |
| SEQ ID NO: 46 | GAG segment 19 | 90 nts |

| SEQUENCE ID NUMBER | SEQ TINGE | LENGTH |
|-----------------------|--------------------------------------|--------|
| SEQ ID NO: 47 | Polypeptide encoded by SEQ ID NO: 46 | 30 aa |
| SEQ ID NO: 48 | GAG segment 20 | 90 nts |
| SEQ ID NO: 49 | Polypeptide encoded by SEQ ID NO: 48 | 30 aa |
| SEQ ID NO: 50 | GAG segment 21 | 90 nts |
| SEQ ID NO: 51 | Polypeptide encoded by SEQ ID NO: 50 | 30 aa |
| SEQ ID NO: 52 | GAG segment 22 | 90 nts |
| SEQ ID NO: 53 | Polypeptide encoded by SEQ ID NO: 52 | 30 aa |
| SEQ ID NO: 54 | GAG segment 23 | 90 nts |
| SEQ ID NO: 55 | Polypeptide encoded by SEQ ID NO: 54 | 30 aa |
| SEQ ID NO: 56 | GAG segment 24 | 90 nts |
| SEQ ID NO: 57 | Polypeptide encoded by SEQ ID NO: 56 | 30 aa |
| SEQ ID NO: 58 | GAG segment 25 | 90 nts |
| SEQ ID NO: 59 | Polypeptide encoded by SEQ ID NO: 58 | 30 aa |
| SEQ ID NO: 60 | GAG segment 26 | 90 nts |
| SEQ ID NO: 61 | Polypeptide encoded by SEQ ID NO: 60 | 30 aa |
| SEQ ID NO: 62 | GAG segment 27 | 90 nts |
| SEQ ID NO: 63 | Polypeptide encoded by SEQ ID NO: 62 | 30 aa |
| SEQ ID NO: 64 | GAG segment 28 | 90 nts |
| SEQ ID NO: 65 | Polypeptide encoded by SEQ ID NO: 64 | 30 aa |
| SEQ ID NO: 66 | GAG segment 29 | 90 nts |
| SEQ ID NO: 67 | Polypeptide encoded by SEQ ID NO: 66 | 30 aa |
| SEQ ID NO: 68 | GAG segment 30 | 90 nts |
| SEQ ID NO: 69 | Polypeptide encoded by SEQ ID NO: 68 | 30 aa |
| SEQ ID NO: 70 | GAG segment 31 | 90 nts |

| SIQUENCI II NUABBR | SEGVENCE | LEVGTH |
|-----------------------|--------------------------------------|--------|
| SEQ ID NO: 71 | Polypeptide encoded by SEQ ID NO: 70 | 30 aa |
| SEQ ID NO: 72 | GAG segment 32 | 90 nts |
| SEQ ID NO: 73 | Polypeptide encoded by SEQ ID NO: 72 | 30 aa |
| SEQ ID NO: 74 | GAG segment 33 | 57 nts |
| SEQ ID NO: 75 | Polypeptide encoded by SEQ ID NO: 74 | 19 aa |
| SEQ ID NO: 76 | POL segment 1 | 90 nts |
| SEQ ID NO: 77 | Polypeptide encoded by SEQ ID NO: 76 | 30 aa |
| SEQ ID NO: 78 | POL segment 2 | 90 nts |
| SEQ ID NO: 79 | Polypeptide encoded by SEQ ID NO: 78 | 30 aa |
| SEQ ID NO: 80 | POL segment 3 | 90 nts |
| SEQ ID NO: 81 | Polypeptide encoded by SEQ ID NO: 80 | 30 aa |
| SEQ ID NO: 82 | POL segment 4 | 90 nts |
| SEQ ID NO: 83 | Polypeptide encoded by SEQ ID NO: 82 | 30 aa |
| SEQ ID NO: 84 | POL segment 5 | 90 nts |
| SEQ ID NO: 85 | Polypeptide encoded by SEQ ID NO: 84 | 30 aa |
| SEQ ID NO: 86 | POL segment 6 | 90 nts |
| SEQ ID NO: 87 | Polypeptide encoded by SEQ ID NO: 86 | 30 aa |
| SEQ ID NO: 88 | POL segment 7 | 90 nts |
| SEQ ID NO: 89 | Polypeptide encoded by SEQ ID NO: 88 | 30 aa |
| SEQ ID NO: 90 | POL segment 8 | 90 nts |
| SEQ ID NO: 91 | Polypeptide encoded by SEQ ID NO: 90 | 30 aa |
| SEQ ID NO: 92 | POL segment 9 | 90 nts |
| SEQ ID NO: 93 | Polypeptide encoded by SEQ ID NO: 92 | 30 aa |
| SEQ ID NO: 94 | POL segment 10 | 90 nts |

| SIQUINCI D NUMBIR | IMQUENCE (| LENGTH |
|-----------------------|---------------------------------------|---------|
| SEQ ID NO: 95 | Polypeptide encoded by SEQ ID NO: 94 | 30 aa |
| SEQ ID NO: 96 | POL segment 11 | 90 nts |
| SEQ ID NO: 97 | Polypeptide encoded by SEQ ID NO: 96 | 30 aa |
| SEQ ID NO: 98 | POL segment 12 | 90 nts |
| SEQ ID NO: 99 | Polypeptide encoded by SEQ ID NO: 98 | 30 aa |
| SEQ ID NO: 100 | POL segment 13 | 90 nts |
| SEQ ID NO: 101 | Polypeptide encoded by SEQ ID NO: 100 | 30 aa |
| SEQ ID NO: 102 | POL segment 14 | 90 nts |
| SEQ ID NO: 103 | Polypeptide encoded by SEQ ID NO: 102 | 30 aa |
| SEQ ID NO: 104 | POL segment 15 | 90 nts |
| SEQ ID NO: 105 | Polypeptide encoded by SEQ ID NO: 104 | 30 aa |
| SEQ ID NO: 106 | POL segment 16 | 90 nts |
| SEQ ID NO: 107 | Polypeptide encoded by SEQ ID NO: 106 | 30 aa |
| SEQ ID NO: 108 | POL segment 17 | 90 nts |
| SEQ ID NO: 109 | Polypeptide encoded by SEQ ID NO: 108 | 30 aa |
| SEQ ID NO: 110 | POL segment 18 | 90 nts |
| SEQ ID NO: 111 | Polypeptide encoded by SEQ ID NO: 110 | 30 aa |
| SEQ ID NO: 112 | POL segment 19 | 90 nts |
| SEQ ID NO: 113 | Polypeptide encoded by SEQ ID NO: 112 | 30 aa |
| SEQ ID NO: 114 | POL segment 20 | 90 nts |
| SEQ ID NO: 115 | Polypeptide encoded by SEQ ID NO: 114 | 30 aa |
| SEQ ID NO: 116 | POL segment 21 | 90 nts |
| SEQ ID NO: 117 | Polypeptide encoded by SEQ ID NO: 116 | · 30 aa |
| SEQ ID NO: 118 | POL segment 22 | 90 nts |

| SOVENCE D | MOUTINGE | LENGTH |
|----------------|---------------------------------------|--------|
| NUMBER. | | |
| SEQ ID NO: 119 | Polypeptide encoded by SEQ ID NO: 118 | 30 aa |
| SEQ ID NO: 120 | POL segment 23 | 90 nts |
| SEQ ID NO: 121 | Polypeptide encoded by SEQ ID NO: 120 | 30 aa |
| SEQ ID NO: 122 | POL segment 24 | 90 nts |
| SEQ ID NO: 123 | Polypeptide encoded by SEQ ID NO: 122 | 30 aa |
| SEQ ID NO: 124 | POL segment 25 | 90 nts |
| SEQ ID NO: 125 | Polypeptide encoded by SEQ ID NO: 124 | 30 aa |
| SEQ ID NO: 126 | POL segment 26 | 90 nts |
| SEQ ID NO: 127 | Polypeptide encoded by SEQ ID NO: 126 | 30 aa |
| SEQ ID NO: 128 | POL segment 27 | 90 nts |
| SEQ ID NO: 129 | Polypeptide encoded by SEQ ID NO: 128 | 30 aa |
| SEQ ID NO: 130 | POL segment 28 | 90 nts |
| SEQ ID NO: 131 | Polypeptide encoded by SEQ ID NO: 130 | 30 aa |
| SEQ ID NO: 132 | POL segment 29 | 90 nts |
| SEQ ID NO: 133 | Polypeptide encoded by SEQ ID NO: 132 | 30 aa |
| SEQ ID NO: 134 | POL segment 30 | 90 nts |
| SEQ ID NO: 135 | Polypeptide encoded by SEQ ID NO: 134 | 30 aa |
| SEQ ID NO: 136 | POL segment 31 | 90 nts |
| SEQ ID NO: 137 | Polypeptide encoded by SEQ ID NO: 136 | 30 aa |
| SEQ ID NO: 138 | POL segment 32 | 90 nts |
| SEQ ID NO: 139 | Polypeptide encoded by SEQ ID NO: 138 | 30 aa |
| SEQ ID NO: 140 | POL segment 33 | 90 nts |
| SEQ ID NO: 141 | Polypeptide encoded by SEQ ID NO: 140 | 30 aa |
| SEQ ID NO: 142 | POL segment 34 | 90 nts |

| DIQUENCI ID NUMBIR | SIGUINCI | . UIMGTH |
|-----------------------|---------------------------------------|----------|
| SEQ ID NO: 143 | Polypeptide encoded by SEQ ID NO: 142 | 30 aa |
| SEQ ID NO: 144 | POL segment 35 | 90 nts |
| SEQ ID NO: 145 | Polypeptide encoded by SEQ ID NO: 144 | 30 aa |
| SEQ ID NO: 146 | POL segment 36 | 90 nts |
| SEQ ID NO: 147 | Polypeptide encoded by SEQ ID NO: 146 | 30 aa |
| SEQ ID NO: 148 | POL segment 37 | 90 nts |
| SEQ ID NO: 149 | Polypeptide encoded by SEQ ID NO: 148 | 30 aa |
| SEQ ID NO: 150 | POL segment 38 | 90 nts |
| SEQ ID NO: 151 | Polypeptide encoded by SEQ ID NO: 150 | 30 aa |
| SEQ ID NO: 152 | POL segment 39 | 90 nts |
| SEQ ID NO: 153 | Polypeptide encoded by SEQ ID NO: 152 | 30 aa |
| SEQ ID NO: 154 | POL segment 40 | 90 nts |
| SEQ ID NO: 155 | Polypeptide encoded by SEQ ID NO: 154 | 30 aa |
| SEQ ID NO: 156 | POL segment 41 | 90 nts |
| SEQ ID NO: 157 | Polypeptide encoded by SEQ ID NO: 156 | 30 aa |
| SEQ ID NO: 158 | POL segment 42 | 90 nts |
| SEQ ID NO: 159 | Polypeptide encoded by SEQ ID NO: 158 | 30 aa |
| SEQ ID NO: 160 | POL segment 43 | 90 nts |
| SEQ ID NO: 161 | Polypeptide encoded by SEQ ID NO: 160 | 30 aa |
| SEQ ID NO: 162 | POL segment 44 | 90 nts |
| SEQ ID NO: 163 | Polypeptide encoded by SEQ ID NO: 162 | .30 aa |
| SEQ ID NO: 164 | POL segment 45 | 90 nts |
| SEQ ID NO: 165 | Polypeptide encoded by SEQ ID NO: 164 | 30 aa |
| SEQ ID NO: 166 | POL segment 46 | 90 nts |

| SEQUENCI NO | IEGUENCE | LENGTH |
|----------------|---------------------------------------|--------|
| NUMBER | <u></u> | |
| SEQ ID NO: 167 | Polypeptide encoded by SEQ ID NO: 166 | 30 aa |
| SEQ ID NO: 168 | POL segment 47 | 90 nts |
| SEQ ID NO: 169 | Polypeptide encoded by SEQ ID NO: 168 | 30 aa |
| SEQ ID NO: 170 | POL segment 48 | 90 nts |
| SEQ ID NO: 171 | Polypeptide encoded by SEQ ID NO: 170 | 30 aa |
| SEQ ID NO: 172 | POL segment 49 | 90 nts |
| SEQ ID NO: 173 | Polypeptide encoded by SEQ ID NO: 172 | 30 aa |
| SEQ ID NO: 174 | POL segment 50 | 90 nts |
| SEQ ID NO: 175 | Polypeptide encoded by SEQ ID NO: 174 | 30 aa |
| SEQ ID NO: 176 | POL segment 51 | 90 nts |
| SEQ ID NO: 177 | Polypeptide encoded by SEQ ID NO: 176 | 30 aa |
| SEQ ID NO: 178 | POL segment 52 | 90 nts |
| SEQ ID NO: 179 | Polypeptide encoded by SEQ ID NO: 178 | 30 aa |
| SEQ ID NO: 180 | POL segment 53 | 90 nts |
| SEQ ID NO: 181 | Polypeptide encoded by SEQ ID NO: 180 | 30 aa |
| SEQ ID NO: 182 | POL segment 54 | 90 nts |
| SEQ ID NO: 183 | Polypeptide encoded by SEQ ID NO: 182 | 30 aa |
| SEQ ID NO: 184 | POL segment 55 | 90 nts |
| SEQ ID NO: 185 | Polypeptide encoded by SEQ ID NO: 184 | 30 aa |
| SEQ ID NO: 186 | POL segment 56 | 90 nts |
| SEQ ID NO: 187 | Polypeptide encoded by SEQ ID NO: 186 | ·30 aa |
| SEQ ID NO: 188 | POL segment 57 | 90 nts |
| SEQ ID NO: 189 | Polypeptide encoded by SEQ ID NO: 188 | 30 aa |
| SEQ ID NO: 190 | POL segment 58 | 90 nts |

| SIQUENCI 10 NUMBER | MEGUENCE | LENGTH |
|-----------------------|---------------------------------------|---------|
| SEQ ID NO: 191 | Polypeptide encoded by SEQ ID NO: 190 | 30 aa |
| SEQ ID NO: 192 | POL segment 59 | 90 nts |
| SEQ ID NO: 193 | Polypeptide encoded by SEQ ID NO: 192 | 30 aa |
| SEQ ID NO: 194 | POL segment 60 | 90 nts |
| SEQ ID NO: 195 | Polypeptide encoded by SEQ ID NO: 194 | 30 aa |
| SEQ ID NO: 196 | POL segment 61 | 90 nts |
| SEQ ID NO: 197 | Polypeptide encoded by SEQ ID NO: 196 | 30 aa |
| SEQ ID NO: 198 | POL segment 62 | 90 nts |
| SEQ ID NO: 199 | Polypeptide encoded by SEQ ID NO: 198 | 30 aa |
| SEQ ID NO: 200 | POL segment 63 | 90 nts |
| SEQ ID NO: 201 | Polypeptide encoded by SEQ ID NO: 200 | 30 aa |
| SEQ ID NO: 202 | POL segment 64 | 90 nts |
| SEQ ID NO: 203 | Polypeptide encoded by SEQ ID NO: 202 | 30 aa |
| SEQ ID NO: 204 | POL segment 65 | 90 nts |
| SEQ ID NO: 205 | Polypeptide encoded by SEQ ID NO: 204 | 30 aa |
| SEQ ID NO: 206 | POL segment 66 | 60 nts |
| SEQ ID NO: 207 | Polypeptide encoded by SEQ ID NO: 206 | 20 aa . |
| SEQ ID NO: 208 | VIF segment 1 | 90 nts |
| SEQ ID NO: 209 | Polypeptide encoded by SEQ ID NO: 208 | 30 aa |
| SEQ ID NO: 210 | VIF segment 2 | 90 nts |
| SEQ ID NO: 211 | Polypeptide encoded by SEQ ID NO: 210 | 30 aa |
| SEQ ID NO: 212 | VIF segment 3 | 90 nts |
| SEQ ID NO: 213 | Polypeptide encoded by SEQ ID NO: 212 | 30 aa |
| SEQ ID NO: 214 | VIF segment 4 | 90 nts |

| SIQUENCI (D NUMBER | SEQUEI CE | LENGTH |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 215 | Polypeptide encoded by SEQ ID NO: 214 | 30 aa |
| SEQ ID NO: 216 | VIF segment 5 | 90 nts |
| SEQ ID NO: 217 | Polypeptide encoded by SEQ ID NO: 216 | 30 aa |
| SEQ ID NO: 218 | VIF segment 6 | 90 nts |
| SEQ ID NO: 219 | Polypeptide encoded by SEQ ID NO: 218 | 30 aa |
| SEQ ID NO: 220 | VIF segment 7 | 90 nts |
| SEQ ID NO: 221 | Polypeptide encoded by SEQ ID NO: 220 | 30 aa |
| SEQ ID NO: 222 | VIF segment 8 | 90 nts |
| SEQ ID NO: 223 | Polypeptide encoded by SEQ ID NO: 222 | 30 aa |
| SEQ ID NO: 224 | VIF segment 9 | 90 nts |
| SEQ ID NO: 225 | Polypeptide encoded by SEQ ID NO: 224 | 30 aa |
| SEQ ID NO: 226 | VIF segment 10 | 90 nts |
| SEQ ID NO: 227 | Polypeptide encoded by SEQ ID NO: 226 | 30 aa |
| SEQ ID NO: 228 | VIF segment 11 | 90 nts |
| SEQ ID NO: 229 | Polypeptide encoded by SEQ ID NO: 228 | 30 aa |
| SEQ ID NO: 230 | VIF segment 12 | 81 nts |
| SEQ ID NO: 231 | Polypeptide encoded by SEQ ID NO: 230 | 27 aa |
| SEQ ID NO: 232 | VPR segment 1 | 90 nts |
| SEQ ID NO: 233 | Polypeptide encoded by SEQ ID NO: 232 | 30 aa |
| SEQ ID NO: 234 | VPR segment 2 | 90 nts |
| SEQ ID NO: 235 | Polypeptide encoded by SEQ ID NO: 234 | 30 aa |
| SEQ ID NO: 236 | VPR segment 3 | 90 nts |
| SEQ ID NO: 237 | Polypeptide encoded by SEQ ID NO: 236 | 30 aa |
| SEQ ID NO: 238 | VPR segment 4 | 90 nts |

| | 27 | |
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| - | Z1 | • |

| SEQUENCE ID | SEGI ENCE | LEMGTH |
|----------------|---------------------------------------|--------|
| MUMBER | | |
| SEQ ID NO: 239 | Polypeptide encoded by SEQ ID NO: 238 | 30 aa |
| SEQ ID NO: 240 | VPR segment 5 | 90 nts |
| SEQ ID NO: 241 | Polypeptide encoded by SEQ ID NO: 240 | 30 aa |
| SEQ ID NO: 242 | VPR segment 6 | 63 nts |
| SEQ ID NO: 243 | Polypeptide encoded by SEQ ID NO: 242 | 21 aa |
| SEQ ID NO: 244 | TAT segment 1 | 90 nts |
| SEQ ID NO: 245 | Polypeptide encoded by SEQ ID NO: 244 | 30 aa |
| SEQ ID NO: 246 | TAT segment 2 | 90 nts |
| SEQ ID NO: 247 | Polypeptide encoded by SEQ ID NO: 246 | 30 aa |
| SEQ ID NO: 248 | TAT segment 3 | 90 nts |
| SEQ ID NO: 249 | Polypeptide encoded by SEQ ID NO: 248 | 30 aa |
| SEQ ID NO: 250 | TAT segment 4 | 90 nts |
| SEQ ID NO: 251 | Polypeptide encoded by SEQ ID NO: 250 | 30 aa |
| SEQ ID NO: 252 | TAT segment 5 | 90 nts |
| SEQ ID NO: 253 | Polypeptide encoded by SEQ ID NO: 252 | 30 aa |
| SEQ ID NO: 254 | TAT segment 6 | 81 nts |
| SEQ ID NO: 255 | Polypeptide encoded by SEQ ID NO: 254 | 27 aa |
| SEQ ID NO: 256 | REV segment 1 | 90 nts |
| SEQ ID NO: 257 | Polypeptide encoded by SEQ ID NO: 256 | 30 aa |
| SEQ ID NO: 258 | REV segment 2 | 90 nts |
| SEQ ID NO: 259 | Polypeptide encoded by SEQ ID NO: 258 | 30 aa |
| SEQ ID NO: 260 | REV segment 3 | 90 nts |
| SEQ ID NO: 261 | Polypeptide encoded by SEQ ID NO: 260 | 30 aa |
| SEQ ID NO: 262 | REV segment 4 | 90 nts |

| ENEROED | SEQUENCE | LIMOTH |
|-----------------------|---------------------------------------|--------|
| NUMBER | | |
| SEQ ID NO: 263 | Polypeptide encoded by SEQ ID NO: 262 | 30 aa |
| SEQ ID NO: 264 | REV segment 5 | 90 nts |
| SEQ ID NO: 265 | Polypeptide encoded by SEQ ID NO: 264 | 30 aa |
| SEQ ID NO: 266 | REV segment 6 | 90 nts |
| SEQ ID NO: 267 | Polypeptide encoded by SEQ ID NO: 266 | 30 aa |
| SEQ ID NO: 268 | REV segment 7 | 90 nts |
| SEQ ID NO: 269 | Polypeptide encoded by SEQ ID NO: 268 | 30 aa |
| SEQ ID NO: 270 | REV segment 8 | 54 nts |
| SEQ ID NO: 271 | Polypeptide encoded by SEQ ID NO: 270 | 18 aa |
| SEQ ID NO: 272 | VPU segment 1 | 90 nts |
| SEQ ID NO: 273 | Polypeptide encoded by SEQ ID NO: 272 | 30 aa |
| SEQ ID NO: 274 | VPU segment 2 | 90 nts |
| SEQ ID NO: 275 | Polypeptide encoded by SEQ ID NO: 274 | 30 aa |
| SEQ ID NO: 276 | VPU segment 3 | 90 nts |
| SEQ ID NO: 277 | Polypeptide encoded by SEQ ID NO: 276 | 30 aa |
| SEQ ID NO: 278 | VPU segment 4 | 90 nts |
| SEQ ID NO: 279 | Polypeptide encoded by SEQ ID NO: 278 | 30 aa |
| SEQ ID NO: 280 | VPU segment 5 | 63 nts |
| SEQ ID NO: 281 | Polypeptide encoded by SEQ ID NO: 280 | 21 aa |
| SEQ ID NO: 282 | ENV segment 1 | 90 nts |
| SEQ ID NO: 283 | Polypeptide encoded by SEQ ID NO: 282 | 30 aa |
| SEQ ID NO: 284 | ENV segment 2 | 90 nts |
| SEQ ID NO: 285 | Polypeptide encoded by SEQ ID NO: 284 | 30 aa |
| SEQ ID NO: 286 | ENV segment 3 | 90 nts |

| SEQUENCE ID MUMBER | SEQUENCE | LENGTH |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 287 | Polypeptide encoded by SEQ ID NO: 286 | 30 aa |
| SEQ ID NO: 288 | ENV segment 4 | 90 nts |
| SEQ ID NO: 289 | Polypeptide encoded by SEQ ID NO: 288 | 30 aa |
| SEQ ID NO: 290 | ENV segment 5 | 90 nts |
| SEQ ID NO: 291 | Polypeptide encoded by SEQ ID NO: 290 | 30 aa |
| SEQ ID NO: 292 | ENV segment 6 | 90 nts |
| SEQ ID NO: 293 | Polypeptide encoded by SEQ ID NO: 292 | 30 aa |
| SEQ ID NO: 294 | ENV segment 7 | 90 nts |
| SEQ ID NO: 295 | Polypeptide encoded by SEQ ID NO: 294 | 30 aa |
| SEQ ID NO: 296 | ENV segment 8 | 90 nts |
| SEQ ID NO: 297 | Polypeptide encoded by SEQ ID NO: 296 | 30 aa |
| SEQ ID NO: 298 | ENV segment 9 | 57 nts |
| SEQ ID NO: 299 | Polypeptide encoded by SEQ ID NO: 298 | 19 aa |
| SEQ ID NO: 300 | GAP A segment 1 | 90 nts |
| SEQ ID NO: 301 | Polypeptide encoded by SEQ ID NO: 300 | 30 aa |
| SEQ ID NO: 302 | GAP A segment 2 | 90 nts |
| SEQ ID NO: 303 | Polypeptide encoded by SEQ ID NO: 302 | 30 aa |
| SEQ ID NO: 304 | GAP A segment 3 | 90 nts |
| SEQ ID NO: 305 | Polypeptide encoded by SEQ ID NO: 304 | 30 aa |
| SEQ ID NO: 306 | GAP A segment 4 | 90 nts |
| SEQ ID NO: 307 | Polypeptide encoded by SEQ ID NO: 306 | 30 aa |
| SEQ ID NO: 308 | GAP A segment 5 | 90 nts |
| SEQ ID NO: 309 | Polypeptide encoded by SEQ ID NO: 308 | 30 aa |
| SEQ ID NO: 310 | GAP A segment 6 | 90 nts |

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| SEGUENCE ID NUMBER | SIGNENCI | LENGTH |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 311 | Polypeptide encoded by SEQ ID NO: 310 | 30 aa |
| SEQ ID NO: 312 | GAP A segment 7 | 75 nts |
| SEQ ID NO: 313 | Polypeptide encoded by SEQ ID NO: 312 | 25 nts |
| SEQ ID NO: 314 | GAP B segment 1 | 90 nts |
| SEQ ID NO: 315 | Polypeptide encoded by SEQ ID NO: 314 | 30 aa |
| SEQ ID NO: 316 | GAP B segment 2 | 90 nts |
| SEQ ID NO: 317 | Polypeptide encoded by SEQ ID NO: 316 | 30 aa |
| SEQ ID NO: 318 | GAP B segment 3 | 90 nts |
| SEQ ID NO: 319 | Polypeptide encoded by SEQ ID NO: 318 | 30 aa |
| SEQ ID NO: 320 | GAP B segment 4 | 90 nts |
| SEQ ID NO: 321 | Polypeptide encoded by SEQ ID NO: 320 | 30 aa |
| SEQ ID NO: 322 | GAP B segment 5 | 90 nts |
| SEQ ID NO: 323 | Polypeptide encoded by SEQ ID NO: 322 | 30 aa |
| SEQ ID NO: 324 | GAP B segment 6 | 90 nts |
| SEQ ID NO: 325 | Polypeptide encoded by SEQ ID NO: 324 | 30 aa |
| SEQ ID NO: 326 | GAP B segment 7 | 90 nts |
| SEQ ID NO: 327 | Polypeptide encoded by SEQ ID NO: 326 | 30 aa |
| SEQ ID NO: 328 | GAP B segment 8 | 90 nts |
| SEQ ID NO: 329 | Polypeptide encoded by SEQ ID NO: 328 | 30 aa |
| SEQ ID NO: 330 | GAP B segment 9 | 90 nts |
| SEQ ID NO: 331 | Polypeptide encoded by SEQ ID NO: 330 | 30 aa |
| SEQ ID NO: 332 | GAP B segment 10 | 90 nts |
| SEQ ID NO: 333 | Polypeptide encoded by SEQ ID NO: 332 | 30 aa |
| SEQ ID NO: 334 | GAP B segment 11 | 90 nts |

| SEGUENCE LD NUMBER | SECENCE | LEXCIH |
|-----------------------|---------------------------------------|----------|
| SEQ ID NO: 335 | Polypeptide encoded by SEQ ID NO: 334 | 30 aa |
| SEQ ID NO: 336 | GAP B segment 12 | 90 nts . |
| SEQ ID NO: 337 | Polypeptide encoded by SEQ ID NO: 336 | 30 aa |
| SEQ ID NO: 338 | GAP B segment 13 | 90 nts |
| SEQ ID NO: 339 | Polypeptide encoded by SEQ ID NO: 338 | 30 aa |
| SEQ ID NO: 340 | GAP B segment 14 | 90 nts |
| SEQ ID NO: 341 | Polypeptide encoded by SEQ ID NO: 340 | 30 aa |
| SEQ ID NO: 342 | GAP B segment 15 | 90 nts |
| SEQ ID NO: 343 | Polypeptide encoded by SEQ ID NO: 342 | 30 aa |
| SEQ ID NO: 344 | GAP B segment 16 | 90 nts |
| SEQ ID NO: 345 | Polypeptide encoded by SEQ ID NO: 344 | 30 aa |
| SEQ ID NO: 346 | GAP B segment 17 | 90 nts |
| SEQ ID NO: 347 | Polypeptide encoded by SEQ ID NO: 346 | 30 aa |
| SEQ ID NO: 348 | GAP B segment 18 | 90 nts |
| SEQ ID NO: 349 | Polypeptide encoded by SEQ ID NO: 348 | 30 aa |
| SEQ ID NO: 350 | GAP B segment 19 | 90 nts |
| SEQ ID NO: 351 | Polypeptide encoded by SEQ ID NO: 350 | 30 aa |
| SEQ ID NO: 352 | GAP B segment 20 | 90 nts |
| SEQ ID NO: 353 | Polypeptide encoded by SEQ ID NO: 352 | 30 aa |
| SEQ ID NO: 354 | GAP B segment 21 | 90 nts |
| SEQ ID NO: 355 | Polypeptide encoded by SEQ ID NO: 354 | 30 aa |
| SEQ ID NO: 356 | GAP B segment 22 | 90 nts |
| SEQ ID NO: 357 | Polypeptide encoded by SEQ ID NO: 356 | 30 aa |
| SEQ ID NO: 358 | GAP B segment 23 | 90 nts |

| SEQUENCE ID NUMBER | SEÇCE: CE | LENGTH |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 359 | Polypeptide encoded by SEQ ID NO: 358 | 30 aa |
| SEQ ID NO: 360 | GAP B segment 24 | 90 nts |
| SEQ ID NO: 361 | Polypeptide encoded by SEQ ID NO: 360 | 30 aa |
| SEQ ID NO: 362 | GAP B segment 25 | 90 nts |
| SEQ ID NO: 363 | Polypeptide encoded by SEQ ID NO: 362 | 30 aa |
| SEQ ID NO: 364 | GAP B segment 26 | 66 nts |
| SEQ ID NO: 365 | Polypeptide encoded by SEQ ID NO: 364 | 22 aa |
| SEQ ID NO: 366 | NEF segment 1 | 90 nts |
| SEQ ID NO: 367 | Polypeptide encoded by SEQ ID NO: 366 | 30 aa |
| SEQ ID NO: 368 | NEF segment 2 | 90 nts |
| SEQ ID NO: 369 | Polypeptide encoded by SEQ ID NO: 368 | 30 aa |
| SEQ ID NO: 370 | NEF segment 3 | 90 nts |
| SEQ ID NO: 371 | Polypeptide encoded by SEQ ID NO: 370 | 30 aa |
| SEQ ID NO: 372 | NEF segment 4 | 90 nts |
| SEQ ID NO: 373 | Polypeptide encoded by SEQ ID NO: 372 | 30 aa |
| SEQ ID NO: 374 | NEF segment 5 | 90 nts |
| SEQ ID NO: 375 | Polypeptide encoded by SEQ ID NO: 374 | 30 aa |
| SEQ ID NO: 376 | NEF segment 6 | 90 nts |
| SEQ ID NO: 377 | Polypeptide encoded by SEQ ID NO: 376 | 30 aa |
| SEQ ID NO: 378 | NEF segment 7 | 90 nts |
| SEQ ID NO: 379 | Polypeptide encoded by SEQ ID NO: 378 | 30 aa |
| SEQ ID NO: 380 | NEF segment 8 | 90 nts |
| SEQ ID NO: 381 | Polypeptide encoded by SEQ ID NO: 380 | 30 aa |
| SEQ ID NO: 382 | NEF segment 9 | 90 nts |

| IEQUENCI D MUNDER | DEQUINCE | LENGTH |
|----------------------|---------------------------------------|-----------|
| SEQ ID NO: 383 | Polypeptide encoded by SEQ ID NO: 382 | 30 aa |
| SEQ ID NO: 384 | NEF segment 10 | 90 nts |
| SEQ ID NO: 385 | Polypeptide encoded by SEQ ID NO: 384 | 30 aa |
| SEQ ID NO: 386 | NEF segment 11 | 90 nts |
| SEQ ID NO: 387 | Polypeptide encoded by SEQ ID NO: 386 | 30 aa |
| SEQ ID NO: 388 | NEF segment 12 | 90 nts |
| SEQ ID NO: 389 | Polypeptide encoded by SEQ ID NO: 388 | 30 aa |
| SEQ ID NO: 390 | NEF segment 13 | 78 nts |
| SEQ ID NO: 391 | Polypeptide encoded by SEQ ID NO: 390 | 26 aa |
| SEQ ID NO: 392 | HIV Cassette A1 | 5703 nts |
| SEQ ID NO: 393 | Polypeptide encoded by SEQ ID NO:392 | 1896 aa |
| SEQ ID NO: 394 | HIV Cassette B1 | 5685 nts |
| SEQ ID NO: 395 | Polypeptide encoded by SEQ ID NO: 394 | 1890 aa |
| SEQ ID NO: 396 | HIV Cassette C1 | 5925 nts |
| SEQ ID NO: 397 | Polypeptide encoded by SEQ ID NO: 396 | 1967 aa |
| SEQ ID NO: 398 | HIV Cassette A2 | 5703 nts |
| SEQ ID NO: 399 | Polypeptide encoded by SEQ ID NO: 398 | 1896 aa |
| SEQ ID NO: 400 | HIV Cassette B2 | 5685 nts |
| SEQ ID NO: 401 | Polypeptide encoded by SEQ ID NO: 400 | 1890 aa |
| SEQ ID NO: 402 | HIV Cassette C2 | 5925 nts |
| SEQ ID NO: 403 | Polypeptide encoded by SEQ ID NO: 402 | 1967 aa |
| SEQ ID NO: 404 | HIV complete Savine | 17244 nts |
| SEQ ID NO: 405 | Polypeptide encoded by SEQ ID NO: 404 | 5747 aa |
| SEQ ID NO: 406 | HepCla consensus polyprotein sequence | 3011 aa |

| SEQUENCE ID NUMBER | SEQUENCE | LENGTH |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 407 | HepCla segment 1 | 90 nts |
| SEQ ID NO: 408 | Polypeptide encoded by SEQ ID NO: 407 | 30 aa |
| SEQ ID NO: 409 | HepC1a segment 2 | 90 nts |
| SEQ ID NO: 410 | Polypeptide encoded by SEQ ID NO: 409 | 30 aa |
| SEQ ID NO: 411 | HepCla segment 3 | 90 nts |
| SEQ ID NO: 412 | Polypeptide encoded by SEQ ID NO: 411 | 30 aa |
| SEQ ID NO: 413 | HepCla segment 4 | 90 nts |
| SEQ ID NO: 414 | Polypeptide encoded by SEQ ID NO: 413 | 30 aa |
| SEQ ID NO: 415 | HepC1a segment 5 | 90 nts |
| SEQ ID NO: 416 | Polypeptide encoded by SEQ ID NO: 415 | 30 aa |
| SEQ ID NO: 417 | HepCla segment 6 | 90 nts |
| SEQ ID NO: 418 | Polypeptide encoded by SEQ ID NO: 417 | 30 aa |
| SEQ ID NO: 419 | HepCla segment 7 | 90 nts |
| SEQ ID NO: 420 | Polypeptide encoded by SEQ ID NO: 419 | 30 aa |
| SEQ ID NO: 421 | HepCla segment 8 | 90 nts |
| SEQ ID NO: 422 | Polypeptide encoded by SEQ ID NO: 421 | 30 aa |
| SEQ ID NO: 423 | HepCla segment 9 | 90 nts |
| SEQ ID NO: 424 | Polypeptide encoded by SEQ ID NO: 423 | 30 aa |
| SEQ ID NO: 425 | HepCla segment 10 | 90 nts |
| SEQ ID NO: 426 | Polypeptide encoded by SEQ ID NO: 425 | 30 aa |
| SEQ ID NO: 427 | HepCla segment 11 | 90 nts |
| SEQ ID NO: 428 | Polypeptide encoded by SEQ ID NO: 427 | 30 aa |
| SEQ ID NO: 429 | HepCla segment 12 | 90 nts |
| SEQ ID NO: 430 | Polypeptide encoded by SEQ ID NO: 429 | 30 aa |

| SIGUENCE ID NUMBER | SEQUENCE. | LENGTH |
|-----------------------|---------------------------------------|---------|
| SEQ ID NO: 431 | HepCla segment 13 | 90 nts |
| SEQ ID NO: 432 | Polypeptide encoded by SEQ ID NO: 431 | 30 aa |
| SEQ ID NO: 433 | HepCla segment 14 | 90 nts |
| SEQ ID NO: 434 | Polypeptide encoded by SEQ ID NO: 433 | 30 aa |
| SEQ ID NO: 435 | HepCla segment 15 | 90 nts |
| SEQ ID NO: 436 | Polypeptide encoded by SEQ ID NO: 435 | 30 aa |
| SEQ ID NO: 437 | HepCla segment 16 | 90 nts |
| SEQ ID NO: 438 | Polypeptide encoded by SEQ ID NO: 437 | 30 aa |
| SEQ ID NO: 439 | HepCla segment 17 | 90 nts |
| SEQ ID NO: 440 | Polypeptide encoded by SEQ ID NO: 439 | 30 aa |
| SEQ ID NO: 441 | HepCla segment 18 | 90 nts |
| SEQ ID NO: 442 | Polypeptide encoded by SEQ ID NO: 441 | 30 aa . |
| SEQ ID NO: 443 | HepC1a segment 19 | 90 nts |
| SEQ ID NO: 444 | Polypeptide encoded by SEQ ID NO: 443 | 30 aa |
| SEQ ID NO: 445 | HepCla segment 20 | 90 nts |
| SEQ ID NO: 446 | Polypeptide encoded by SEQ ID NO: 445 | 30 aa |
| SEQ ID NO: 447 | HepC1a segment 21 | 90 nts |
| SEQ ID NO: 448 | Polypeptide encoded by SEQ ID NO: 447 | 30 aa |
| SEQ ID NO: 449 | HepC1a segment 22 | 90 nts |
| SEQ ID NO: 450 | Polypeptide encoded by SEQ ID NO: 449 | 30 aa |
| SEQ ID NO: 451 | HepC1a segment 23 | 90 nts |
| SEQ ID NO: 452 | Polypeptide encoded by SEQ ID NO: 451 | 30 aa |
| SEQ ID NO: 453 | HepCla segment 24 | 90 nts |
| SEQ ID NO: 454 | Polypeptide encoded by SEQ ID NO: 453 | 30 aa |

| SEQUENCE IN NUMBER | TOU. I | LENGDI |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 455 | HepCla segment 25 | 90 nts |
| SEQ ID NO: 456 | Polypeptide encoded by SEQ ID NO: 455 | 30 aa |
| SEQ ID NO: 457 | HepC1a segment 26 | 90 nts |
| SEQ ID NO: 458 | Polypeptide encoded by SEQ ID NO: 457 | 30 aa |
| SEQ ID NO: 459 | HepC1a segment 27 | 90 nts |
| SEQ ID NO: 460 | Polypeptide encoded by SEQ ID NO: 459 | 30 aa |
| SEQ ID NO: 461 | HepC1a segment 28 | 90 nts |
| SEQ ID NO: 462 | Polypeptide encoded by SEQ ID NO: 461 | 30 aa |
| SEQ ID NO: 463 | HepCla segment 29 | 90 nts |
| SEQ ID NO: 464 | Polypeptide encoded by SEQ ID NO: 463 | 30 aa |
| SEQ ID NO: 465 | HepCla segment 30 | 90 nts |
| SEQ ID NO: 466 | Polypeptide encoded by SEQ ID NO: 465 | 30 aa |
| SEQ ID NO: 467 | HepCla segment 31 | 90 nts |
| SEQ ID NO: 468 | Polypeptide encoded by SEQ ID NO: 467 | 30 aa |
| SEQ ID NO: 469 | HepC1a segment 32 | 90 nts |
| SEQ ID NO: 470 | Polypeptide encoded by SEQ ID NO: 469 | 30 aa |
| SEQ ID NO: 471 | HepC1a segment 33 | 90 nts |
| SEQ ID NO: 472 | Polypeptide encoded by SEQ ID NO: 471 | 30 aa |
| SEQ ID NO: 473 | HepCla segment 34 | 90 nts |
| SEQ ID NO: 474 | Polypeptide encoded by SEQ ID NO: 473 | 30 aa |
| SEQ ID NO: 475 | HepCla segment 35 | 90 nts |
| SEQ ID NO: 476 | Polypeptide encoded by SEQ ID NO: 475 | 30 aa |
| SEQ ID NO: 477 | HepCla segment 36 | 90 nts |
| SEQ ID NO: 478 | Polypeptide encoded by SEQ ID NO: 477 | 30 aa |

| SECUTINCI ID NUMBER | SEQUENCE | LENGTH |
|------------------------|---------------------------------------|--------|
| SEQ ID NO: 479 | HepCla segment 37 | 90 nts |
| SEQ ID NO: 480 | Polypeptide encoded by SEQ ID NO: 479 | 30 aa |
| SEQ ID NO: 481 | HepCla segment 38 | 90 nts |
| SEQ ID NO: 482 | Polypeptide encoded by SEQ ID NO: 481 | 30 aa |
| SEQ ID NO: 483 | HepCla segment 39 | 90 nts |
| SEQ ID NO: 484 | Polypeptide encoded by SEQ ID NO: 483 | 30 aa |
| SEQ ID NO: 485 | HepCla segment 40 | 90 nts |
| SEQ ID NO: 486 | Polypeptide encoded by SEQ ID NO: 485 | 30 aa |
| SEQ ID NO: 487 | HepC1a segment 41 | 90 nts |
| SEQ ID NO: 488 | Polypeptide encoded by SEQ ID NO: 487 | 30 aa |
| SEQ ID NO: 489 | HepC1a segment 42 | 90 nts |
| SEQ ID NO: 490 | Polypeptide encoded by SEQ ID NO: 489 | 30 aa |
| SEQ ID NO: 491 | HepCla segment 43 | 90 nts |
| SEQ ID NO: 492 | Polypeptide encoded by SEQ ID NO: 491 | 30 aa |
| SEQ ID NO: 493 | HepCla segment 44 | 90 nts |
| SEQ ID NO: 494 | Polypeptide encoded by SEQ ID NO: 493 | 30 aa |
| SEQ ID NO: 495 | HepCla segment 45 | 90 nts |
| SEQ ID NO: 496 | Polypeptide encoded by SEQ ID NO: 495 | 30 aa |
| SEQ ID NO: 497 | HepCla segment 46 | 90 nts |
| SEQ ID NO: 498 | Polypeptide encoded by SEQ ID NO: 497 | 30 aa |
| SEQ ID NO: 499 | HepCla segment 47 | 90 nts |
| SEQ ID NO: 500 | Polypeptide encoded by SEQ ID NO: 499 | 30 aa |
| SEQ ID NO: 501 | HepCla segment 48 | 90 nts |
| SEQ ID NO: 502 | Polypeptide encoded by SEQ ID NO: 501 | 30 aa |

| SEQUENCE D NUMBER | SEQUENCE | LENGTH |
|----------------------|---------------------------------------|---------|
| SEQ ID NO: 503 | HepC1a segment 49 | 90 nts |
| SEQ ID NO: 504 | Polypeptide encoded by SEQ ID NO: 503 | 30 aa |
| SEQ ID NO: 505 | HepC1a segment 50 | 90 nts |
| SEQ ID NO: 506 | Polypeptide encoded by SEQ ID NO: 505 | 30 aa |
| SEQ ID NO: 507 | HepC1a segment 51 | 90 nts |
| SEQ ID NO: 508 | Polypeptide encoded by SEQ ID NO: 507 | 30 aa |
| SEQ ID NO: 509 | HepCla segment 52 | .90 nts |
| SEQ ID NO: 510 | Polypeptide encoded by SEQ ID NO: 509 | 30 aa |
| SEQ ID NO: 511 | HepCla segment 53 | 90 nts |
| SEQ ID NO: 512 | Polypeptide encoded by SEQ ID NO: 511 | 30 aa |
| SEQ ID NO: 513 | HepC1a segment 54 | 90 nts |
| SEQ ID NO: 514 | Polypeptide encoded by SEQ ID NO: 513 | 30 aa |
| SEQ ID NO: 515 | HepC1a segment 55 | 90 nts |
| SEQ ID NO: 516 | Polypeptide encoded by SEQ ID NO: 515 | 30 aa |
| SEQ ID NO: 517 | HepCla segment 56 | 90 nts |
| SEQ ID NO: 518 | Polypeptide encoded by SEQ ID NO: 517 | 30 aa |
| SEQ ID NO: 519 | HepC1a segment 57 | 90 nts |
| SEQ ID NO: 520 | Polypeptide encoded by SEQ ID NO: 519 | 30 aa |
| SEQ ID NO: 521 | HepCla segment 58 | 90 nts |
| SEQ ID NO: 522 | Polypeptide encoded by SEQ ID NO: 521 | 30 aa |
| SEQ ID NO: 523 | HepCla segment 59 | 90 nts |
| SEQ ID NO: 524 | Polypeptide encoded by SEQ ID NO: 523 | 30 aa |
| SEQ ID NO: 525 | HepCla segment 60 | 90 nts |
| SEQ ID NO: 526 | Polypeptide encoded by SEQ ID NO: 525 | 30 aa |

| SEQUENCE ID NUMBER | SIGUENCE | LENGTH |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 527 | HepCla segment 61 | 90 nts |
| SEQ ID NO: 528 | Polypeptide encoded by SEQ ID NO: 527 | 30 aa |
| SEQ ID NO: 529 | HepCla segment 62 | 90 nts |
| SEQ ID NO: 530 | Polypeptide encoded by SEQ ID NO: 529 | 30 aa |
| SEQ ID NO: 531 | HepCla segment 63 | 90 nts |
| SEQ ID NO: 532 | Polypeptide encoded by SEQ ID NO: 531 | 30 aa |
| SEQ ID NO: 533 | HepC1a segment 64 | 90 nts |
| SEQ ID NO: 534 | Polypeptide encoded by SEQ ID NO: 533 | 30 aa |
| SEQ ID NO: 535 | HepCla segment 65 | 90 nts |
| SEQ ID NO: 536 | Polypeptide encoded by SEQ ID NO: 535 | 30 aa |
| SEQ ID NO: 537 | HepC1a segment 66 | 90 nts |
| SEQ ID NO: 538 | Polypeptide encoded by SEQ ID NO: 537 | 30 aa |
| SEQ ID NO: 539 | HepCla segment 67 | 90 nts |
| SEQ ID NO: 540 | Polypeptide encoded by SEQ ID NO: 539 | 30 aa |
| SEQ ID NO: 541 | HepCla segment 68 | 90 nts |
| SEQ ID NO: 542 | Polypeptide encoded by SEQ ID NO: 541 | 30 aa |
| SEQ ID NO: 543 | HepCla segment 69 | 90 nts |
| SEQ ID NO: 544 | Polypeptide encoded by SEQ ID NO: 543 | 30 aa |
| SEQ ID NO: 545 | HepCla segment 70 | 90 nts |
| SEQ ID NO: 546 | Polypeptide encoded by SEQ ID NO:545 | 30 aa |
| SEQ ID NO: 547 | HepCla segment 71 | 90 nts |
| SEQ ID NO: 548 | Polypeptide encoded by SEQ ID NO: 547 | 30 aa |
| SEQ ID NO: 549 | HepCla segment 72 | 90 nts |
| SEQ ID NO: 550 | Polypeptide encoded by SEQ ID NO: 549 | 30 aa |

| SEQUENCE D NUABUR | NOVENCE | LENGTH |
|----------------------|---------------------------------------|--------|
| SEQ ID NO: 551 | HepC1a segment 73 | 90 nts |
| SEQ ID NO: 552 | Polypeptide encoded by SEQ ID NO: 551 | 30 aa |
| SEQ ID NO: 553 | HepCla segment 74 | 90 nts |
| SEQ ID NO: 554 | Polypeptide encoded by SEQ ID NO: 553 | 30 aa |
| SEQ ID NO: 555 | HepCla segment 75 | 90 nts |
| SEQ ID NO: 556 | Polypeptide encoded by SEQ ID NO: 555 | 30 aa |
| SEQ ID NO: 557 | HepCla segment 76 | 90 nts |
| SEQ ID NO: 558 | Polypeptide encoded by SEQ ID NO: 557 | 30 aa |
| SEQ ID NO: 559 | HepCla segment 77 | 90 nts |
| SEQ ID NO: 560 | Polypeptide encoded by SEQ ID NO: 559 | 30 aa |
| SEQ ID NO: 561 | HepCla segment 78 | 90 nts |
| SEQ ID NO: 562 | Polypeptide encoded by SEQ ID NO: 561 | 30 aa |
| SEQ ID NO: 563 | HepCla segment 79 | 90 nts |
| SEQ ID NO: 564 | Polypeptide encoded by SEQ ID NO: 563 | 30 aa |
| SEQ ID NO: 565 | HepCla segment 80 | 90 nts |
| SEQ ID NO: 566 | Polypeptide encoded by SEQ ID NO: 565 | 30 aa |
| SEQ ID NO: 567 | HepCla segment 81 | 90 nts |
| SEQ ID NO: 568 | Polypeptide encoded by SEQ ID NO: 567 | 30 aa |
| SEQ ID NO: 569 | HepCla segment 82 | 90 nts |
| SEQ ID NO: 570 | Polypeptide encoded by SEQ ID NO: 569 | 30 aa |
| SEQ ID NO: 571 | HepC1a segment 83 | 90 nts |
| SEQ ID NO: 572 | Polypeptide encoded by SEQ ID NO: 571 | 30 aa |
| SEQ ID NO: 573 | HepCla segment 84 | 90 nts |
| SEQ ID NO: 574 | Polypeptide encoded by SEQ ID NO: 573 | 30 aa |

| SIQUENCI 10 NUMBER | SEGUENCE | LINGTH |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 575 | HepC1a segment 85 | 90 nts |
| SEQ ID NO: 576 | Polypeptide encoded by SEQ ID NO: 575 | 30 aa |
| SEQ ID NO: 577 | HepC1a segment 86 | 90 nts |
| SEQ ID NO: 578 | Polypeptide encoded by SEQ ID NO: 577 | 30 aa |
| SEQ ID NO: 579 | HepCla segment 87 | 90 nts |
| SEQ ID NO: 580 | Polypeptide encoded by SEQ ID NO: 579 | 30 aa |
| SEQ ID NO: 581 | HepC1a segment 88 | 90 nts |
| SEQ ID NO: 582 | Polypeptide encoded by SEQ ID NO: 581 | 30 aa |
| SEQ ID NO: 583 | HepC1a segment 89 | 90 nts |
| SEQ ID NO: 584 | Polypeptide encoded by SEQ ID NO: 583 | 30 aa |
| SEQ ID NO: 585 | HepC1a segment 90 | 90 nts |
| SEQ ID NO: 586 | Polypeptide encoded by SEQ ID NO: 585 | 30 aa |
| SEQ ID NO: 587 | HepC1a segment 91 | 90 nts |
| SEQ ID NO: 588 | Polypeptide encoded by SEQ ID NO: 587 | 30 aa |
| SEQ ID NO: 589 | HepC1a segment 92 | 90 nts |
| SEQ ID NO: 590 | Polypeptide encoded by SEQ ID NO: 589 | 30 aa |
| SEQ ID NO: 591 | HepCla segment 93 | 90 nts |
| SEQ ID NO: 592 | Polypeptide encoded by SEQ ID NO: 591 | 30 aa |
| SEQ ID NO: 593 | HepCla segment 94 | 90 nts |
| SEQ ID NO: 594 | Polypeptide encoded by SEQ ID NO: 593 | 30 aa |
| SEQ ID NO: 595 | HepCla segment 95 | 90 nts |
| SEQ ID NO: 596 | Polypeptide encoded by SEQ ID NO: 595 | 30 aa |
| SEQ ID NO: 597 | HepCla segment 96 | 90 nts |
| SEQ ID NO: 598 | Polypeptide encoded by SEQ ID NO: 597 | 30 aa |

| SEQUENCE ID NUMBER | MONEYCE | LENGTH |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 599 | HepC1a segment 97 | 90 nts |
| SEQ ID NO: 600 | Polypeptide encoded by SEQ ID NO: 599 | 30 aa |
| SEQ ID NO: 601 | HepCla segment 98 | 90 nts |
| SEQ ID NO: 602 | Polypeptide encoded by SEQ ID NO: 601 | 30 aa |
| SEQ ID NO: 603 | HepCla segment 99 | 90 nts |
| SEQ ID NO: 604 | Polypeptide encoded by SEQ ID NO: 603 | 30 aa |
| SEQ ID NO: 605 | HepCla segment 100 | 90 nts |
| SEQ ID NO: 606 | Polypeptide encoded by SEQ ID NO: 605 | 30 aa |
| SEQ ID NO: 607 | HepC1a segment 101 | 90 nts |
| SEQ ID NO: 608 | Polypeptide encoded by SEQ ID NO: 607 | 30 aa |
| SEQ ID NO: 609 | HepC1a segment 102 | 90 nts |
| SEQ ID NO: 610 | Polypeptide encoded by SEQ ID NO: 609 | 30 aa |
| SEQ ID NO: 611 | HepC1a segment 103 | 90 nts |
| SEQ ID NO: 612 | Polypeptide encoded by SEQ ID NO: 611 | 30 aa |
| SEQ ID NO: 613 | HepC1a segment 104 | 90 nts |
| SEQ ID NO: 614 | Polypeptide encoded by SEQ ID NO: 613 | 30 aa |
| SEQ ID NO: 615 | HepCla segment 105 | 90 nts |
| SEQ ID NO: 616 | Polypeptide encoded by SEQ ID NO: 615 | 30 aa |
| SEQ ID NO: 617 | HepCla segment 106 | 90 nts |
| SEQ ID NO: 618 | Polypeptide encoded by SEQ ID NO: 617 | 30 aa |
| SEQ ID NO: 619 | HepCla segment 107 | 90 nts |
| SEQ ID NO: 620 | Polypeptide encoded by SEQ ID NO: 619 | 30 aa |
| SEQ ID NO: 621 | HepCla segment 108 | 90 nts |
| SEQ ID NO: 622 | Polypeptide encoded by SEQ ID NO: 621 | 30 aa |

| SEQUENCE D NUABER | SEQUENCE | LENGTH |
|-----------------------|---------------------------------------|---------|
| SEQ ID NO: 623 | HepCla segment 109 | 90 nts |
| SEQ ID NO: 624 | Polypeptide encoded by SEQ ID NO: 623 | 30 aa |
| SEQ ID NO: 625 | HepC1a segment 110 | 90 nts |
| SEQ ID NO: 626 | Polypeptide encoded by SEQ ID NO: 625 | 30 aa |
| SEQ ID NO: 627 | HepCla segment 111 | 90 nts |
| SEQ ID NO: 628 | Polypeptide encoded by SEQ ID NO: 627 | 30 aa |
| SEQ ID NO: 629 | HepCla segment 112 | 90 nts |
| SEQ ID NO: 630 | Polypeptide encoded by SEQ ID NO: 629 | 30 aa |
| SEQ ID NO: 631 | HepCla segment 113 | 90 nts |
| SEQ ID NO: 632 | Polypeptide encoded by SEQ ID NO: 631 | 30 aa |
| SEQ ID NO: 633 | HepCla segment 114 | 90 nts |
| SEQ ID NO: 634 | Polypeptide encoded by SEQ ID NO: 633 | 30 aa |
| SEQ ID NO: 635 | HepCla segment 115 | 90 nts |
| SEQ ID NO: 636 | Polypeptide encoded by SEQ ID NO: 635 | 30 aa |
| SEQ ID NO: 637 | HepCla segment 116 | 90 nts |
| SEQ ID NO: 638 | Polypeptide encoded by SEQ ID NO: 637 | 30 aa |
| SEQ ID NO: 639 | HepCla segment 117 | 90 nts |
| SEQ ID NO: 640 | Polypeptide encoded by SEQ ID NO: 639 | 30 aa |
| SEQ ID NO: 641 | HepCla segment 118 | 90 nts |
| SEQ ID NO: 642 | Polypeptide encoded by SEQ ID NO: 641 | 30 aa |
| SEQ ID NO: 643 | HepCla segment 119 | .90 nts |
| SEQ ID NO: 644 | Polypeptide encoded by SEQ ID NO: 643 | 30 aa |
| SEQ ID NO: 645 | HepCla segment 120 | 90 nts |
| SEQ ID NO: 646 | Polypeptide encoded by SEQ ID NO: 645 | 30 aa |

| SEQUENCE ID NUMBER | ! SEQUENCE | LENGTH |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 647 | HepCla segment 121 | 90 nts |
| SEQ ID NO: 648 | Polypeptide encoded by SEQ ID NO: 647 | 30 aa |
| SEQ ID NO: 649 | HepC1a segment 122 | 90 nts |
| SEQ ID NO: 650 | Polypeptide encoded by SEQ ID NO: 649 | 30 aa |
| SEQ ID NO: 651 | HepC1a segment 123 | 90 nts |
| SEQ ID NO: 652 | Polypeptide encoded by SEQ ID NO: 651 | 30 aa |
| SEQ ID NO: 653 | HepC1a segment 124 | 90 nts |
| SEQ ID NO: 654 | Polypeptide encoded by SEQ ID NO: 653 | 30 aa |
| SEQ ID NO: 655 | HepCla segment 125 | 90 nts |
| SEQ ID NO: 656 | Polypeptide encoded by SEQ ID NO: 655 | 30 aa |
| SEQ ID NO: 657 | HepCla segment 126 | 90 nts |
| SEQ ID NO: 658 | Polypeptide encoded by SEQ ID NO: 657 | 30 aa |
| SEQ ID NO: 659 | HepCla segment 127 | 90 nts |
| SEQ ID NO: 660 | Polypeptide encoded by SEQ ID NO: 659 | 30 aa |
| SEQ ID NO: 661 | HepCla segment 128 | 90 nts |
| SEQ ID NO: 662 | Polypeptide encoded by SEQ ID NO: 661 | 30 aa |
| SEQ ID NO: 663 | HepC1a segment 129 | 90 nts |
| SEQ ID NO: 664 | Polypeptide encoded by SEQ ID NO: 663 | 30 aa |
| SEQ ID NO: 665 | HepC1a segment 130 | 90 nts |
| SEQ ID NO: 666 | Polypeptide encoded by SEQ ID NO: 665 | 30 aa |
| SEQ ID NO: 667 | HepCla segment 131 | 90 nts |
| SEQ ID NO: 668 | Polypeptide encoded by SEQ ID NO: 667 | 30 aa |
| SEQ ID NO: 669 | HepC1a segment 132 | 90 nts |
| SEQ ID NO: 670 | Polypeptide encoded by SEQ ID NO: 669 | 30 aa |

| SEQUENCE ID NUMBER | e Seguence i | LENGTH |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 671 | HepC1a segment 133 | 90 nts |
| SEQ ID NO: 672 | Polypeptide encoded by SEQ ID NO: 671 | 30 aa |
| SEQ ID NO: 673 | HepC1a segment 134 | 90 nts |
| SEQ ID NO: 674 | Polypeptide encoded by SEQ ID NO: 673 | 30 aa |
| SEQ ID NO: 675 | HepC1a segment 135 | 90 nts |
| SEQ ID NO: 676 | Polypeptide encoded by SEQ ID NO: 675 | 30 aa |
| SEQ ID NO: 677 | HepC1a segment 136 | 90 nts |
| SEQ ID NO: 678 | Polypeptide encoded by SEQ ID NO: 677 | 30 aa |
| SEQ ID NO: 679 | HepC1a segment 137 | 90 nts |
| SEQ ID NO: 680 | Polypeptide encoded by SEQ ID NO: 679 | 30 aa |
| SEQ ID NO: 681 | HepC1a segment 138 | 90 nts |
| SEQ ID NO: 682 | Polypeptide encoded by SEQ ID NO: 681 | 30 aa |
| SEQ ID NO: 683 | HepC1a segment 139 | 90 nts |
| SEQ ID NO: 684 | Polypeptide encoded by SEQ ID NO: 683 | 30 aa |
| SEQ ID NO: 685 | HepC1a segment 140 | 90 nts |
| SEQ ID NO: 686 | Polypeptide encoded by SEQ ID NO: 685 | 30 aa |
| SEQ ID NO: 687 | HepCla segment 141 | 90 nts |
| SEQ ID NO: 688 | Polypeptide encoded by SEQ ID NO: 687 | 30 aa |
| SEQ ID NO: 689 | HcpC1a segment 142 | 90 nts |
| SEQ ID NO: 690 | Polypeptide encoded by SEQ ID NO: 689 | 30 aa |
| SEQ ID NO: 691 | HepCla segment 143 | 90 nts |
| SEQ ID NO: 692 | Polypeptide encoded by SEQ ID NO: 691 | 30 aa |
| SEQ ID NO: 693 | HepC1a segment 144 | 90 nts |
| SEQ ID NO: 694 | Polypeptide encoded by SEQ ID NO: 693 | 30 aa |

| SIGUENCE D NUMBER | SIQUENCI | LINGTH |
|----------------------|---------------------------------------|--------|
| SEQ ID NO: 695 | HepCla segment 145 | 90 nts |
| SEQ ID NO: 696 | Polypeptide encoded by SEQ ID NO: 695 | 30 aa |
| SEQ ID NO: 697 | HepCla segment 146 | 90 nts |
| SEQ ID NO: 698 | Polypeptide encoded by SEQ ID NO: 697 | 30 aa |
| SEQ ID NO: 699 | HepCla segment 147 | 90 nts |
| SEQ ID NO: 700 | Polypeptide encoded by SEQ ID NO: 699 | 30 aa |
| SEQ ID NO: 701 | HepCla segment 148 | 90 nts |
| SEQ ID NO: 702 | Polypeptide encoded by SEQ ID NO: 701 | 30 aa |
| SEQ ID NO: 703 | HepC1a segment 149 | 90 nts |
| SEQ ID NO: 704 | Polypeptide encoded by SEQ ID NO: 703 | 30 aa |
| SEQ ID NO: 705 | HepC1a segment 150 | 90 nts |
| SEQ ID NO: 706 | Polypeptide encoded by SEQ ID NO: 705 | 30 aa |
| SEQ ID NO: 707 | HepCla segment 151 | 90 nts |
| SEQ ID NO: 708 | Polypeptide encoded by SEQ ID NO: 707 | 30 aa |
| SEQ ID NO: 709 | HepC1a segment 152 | 90 nts |
| SEQ ID NO: 710 | Polypeptide encoded by SEQ ID NO: 709 | 30 aa |
| SEQ ID NO: 711 | HepC1a segment 153 | 90 nts |
| SEQ ID NO: 712 | Polypeptide encoded by SEQ ID NO: 711 | 30 aa |
| SEQ ID NO: 713 | HepCla segment 154 | 90 nts |
| SEQ ID NO: 714 | Polypeptide encoded by SEQ ID NO: 713 | 30 aa |
| SEQ ID NO: 715 | HepCla segment 155 | 90 nts |
| SEQ ID NO: 716 | Polypeptide encoded by SEQ ID NO: 715 | 30 aa |
| SEQ ID NO: 717 | HepCla segment 156 | 90 nts |
| SEQ ID NO: 718 | Polypeptide encoded by SEQ ID NO: 717 | 30 aa |

| SEQUENCE ID NUMBER | SEQUENCE | LINGTH |
|-----------------------|---------------------------------------|---------|
| SEQ ID NO: 719 | HepCla segment 157 | 90 nts |
| SEQ ID NO: 720 | Polypeptide encoded by SEQ ID NO: 719 | 30 aa |
| SEQ ID NO: 721 | HepCla segment 158 | 90 nts |
| SEQ ID NO: 722 | Polypeptide encoded by SEQ ID NO: 721 | 30 aa |
| SEQ ID NO: 723 | HepC1a segment 159 | 90 nts |
| SEQ ID NO: 724 | Polypeptide encoded by SEQ ID NO: 723 | 30 aa |
| SEQ ID NO: 725 | HepCla segment 160 | 90 nts |
| SEQ ID NO: 726 | Polypeptide encoded by SEQ ID NO: 725 | 30 aa |
| SEQ ID NO: 727 | HepCla segment 161 | 90 nts |
| SEQ ID NO: 728 | Polypeptide encoded by SEQ ID NO: 727 | 30 aa |
| SEQ ID NO: 729 | HepC1a segment 162 | 90 nts |
| SEQ ID NO: 730 | Polypeptide encoded by SEQ ID NO: 729 | 30 aa |
| SEQ ID NO: 731 | HepC1a segment 163 | 90 nts |
| SEQ ID NO: 732 | Polypeptide encoded by SEQ ID NO: 731 | 30 aa |
| SEQ ID NO: 733 | HepC1a segment 164 | 90 nts |
| SEQ ID NO: 734 | Polypeptide encoded by SEQ ID NO: 733 | 30 aa |
| SEQ ID NO: 735 | HepC1a segment 165 | 90 nts |
| SEQ ID NO: 736 | Polypeptide encoded by SEQ ID NO: 735 | 30 aa |
| SEQ ID NO: 737 | HepCla segment 166 | 90 nts |
| SEQ ID NO: 738 | Polypeptide encoded by SEQ ID NO: 737 | 30 aa |
| SEQ ID NO: 739 | HepCla segment 167 | .90 nts |
| SEQ ID NO: 740 | Polypeptide encoded by SEQ ID NO: 739 | 30 aa |
| SEQ ID NO: 741 | HepCla segment 168 | 90 nts |
| SEQ ID NO: 742 | Polypeptide encoded by SEQ ID NO: 741 | 30 aa |

| NEQUENCE ID NUMBER | SEQUENCE | LENGTH |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 743 | HepCla segment 169 | 90 nts |
| SEQ ID NO: 744 | Polypeptide encoded by SEQ ID NO: 743 | 30 aa |
| SEQ ID NO: 745 | HepCla segment 170 | 90 nts |
| SEQ ID NO: 746 | Polypeptide encoded by SEQ ID NO: 745 | 30 aa |
| SEQ ID NO: 747 | HepCla segment 171 | 90 nts |
| SEQ ID NO: 748 | Polypeptide encoded by SEQ ID NO: 747 | 30 aa |
| SEQ ID NO: 749 | HepC1a segment 172 | 90 nts |
| SEQ ID NO: 750 | Polypeptide encoded by SEQ ID NO: 749 | 30 aa |
| SEQ ID NO: 751 | HepC1a segment 173 | 90 nts |
| SEQ ID NO: 752 | Polypeptide encoded by SEQ ID NO: 751 | 30 aa |
| SEQ ID NO: 753 | HepCla segment 174 | 90 nts |
| SEQ ID NO: 754 | Polypeptide encoded by SEQ ID NO: 753 | 30 aa |
| SEQ ID NO: 755 | HepCla segment 175 | 90 nts |
| SEQ ID NO: 756 | Polypeptide encoded by SEQ ID NO: 755 | 30 aa |
| SEQ ID NO: 757 | HepCla segment 176 | 90 nts |
| SEQ ID NO: 758 | Polypeptide encoded by SEQ ID NO: 757 | 30 aa |
| SEQ ID NO: 759 | HepCla segment 177 | 90 nts |
| SEQ ID NO: 760 | Polypeptide encoded by SEQ ID NO: 759 | 30 aa |
| SEQ ID NO: 761 | HepCla segment 178 | 90 nts |
| SEQ ID NO: 762 | Polypeptide encoded by SEQ ID NO: 761 | 30 aa |
| SEQ ID NO: 763 | HepCla segment 179 | 90 nts |
| SEQ ID NO: 764 | Polypeptide encoded by SEQ ID NO: 763 | 30 aa |
| SEQ ID NO: 765 | HepCla segment 180 | 90 nts |
| SEQ ID NO: 766 | Polypeptide encoded by SEQ ID NO: 765 | 30 aa |

| SEQUENCE ED NUMBER | MQUEVCI | LENGTH |
|-----------------------|---------------------------------------|----------|
| SEQ ID NO: 767 | HepCla segment 181 | 90 nts |
| SEQ ID NO: 768 | Polypeptide encoded by SEQ ID NO: 767 | 30 aa |
| SEQ ID NO: 769 | HepCla segment 182 | 90 nts · |
| SEQ ID NO: 770 | Polypeptide encoded by SEQ ID NO: 769 | 30 aa |
| SEQ ID NO: 771 | HepC1a segment 183 | 90 nts |
| SEQ ID NO: 772 | Polypeptide encoded by SEQ ID NO: 771 | ·30 aa |
| SEQ ID NO: 773 | HepCla segment 184 | 90 nts |
| SEQ ID NO: 774 | Polypeptide encoded by SEQ ID NO: 773 | 30 aa |
| SEQ ID NO: 775 | HepC1a segment 185 | 90 nts |
| SEQ ID NO: 776 | Polypeptide encoded by SEQ ID NO: 775 | 30 aa |
| SEQ ID NO: 777 | HepCla segment 186 | 90 nts |
| SEQ ID NO: 778 | Polypeptide encoded by SEQ ID NO: 777 | 30 aa |
| SEQ ID NO: 779 | HepCla segment 187 | 90 nts |
| SEQ ID NO: 780 | Polypeptide encoded by SEQ ID NO: 779 | 30 aa |
| SEQ ID NO: 781 | HepCla segment 188 | 90 nts |
| SEQ ID NO: 782 | Polypeptide encoded by SEQ ID NO: 781 | 30 aa |
| SEQ ID NO: 783 | HepCla segment 189 | 90 nts |
| SEQ ID NO: 784 | Polypeptide encoded by SEQ ID NO: 783 | 30 aa |
| SEQ ID NO: 785 | HepCla segment 190 | 90 nts |
| SEQ ID NO: 786 | Polypeptide encoded by SEQ ID NO: 785 | 30 aa |
| SEQ ID NO: 787 | HepCla segment 191 | 90 nts |
| SEQ ID NO: 788 | Polypeptide encoded by SEQ ID NO: 787 | 30 aa |
| SEQ ID NO: 789 | HepCla segment 192 | 90 nts |
| SEQ ID NO: 790 | Polypeptide encoded by SEQ ID NO: 789 | 30 aa |

| SEQUENCE ID NUMBER | SEQUENCE | LENGTH |
|-----------------------|---------------------------------------|-----------|
| SEQ ID NO: 791 | HepC1a segment 193 | 90 nts |
| SEQ ID NO: 792 | Polypeptide encoded by SEQ ID NO: 791 | 30 aa |
| SEQ ID NO: 793 | HepCla segment 194 | 90 nts |
| SEQ ID NO: 794 | Polypeptide encoded by SEQ ID NO: 793 | 30 aa |
| SEQ ID NO: 795 | HepCla segment 195 | 90 nts |
| SEQ ID NO: 796 | Polypeptide encoded by SEQ ID NO: 795 | 30 aa |
| SEQ ID NO: 797 | HepC1a segment 196 | 90 nts |
| SEQ ID NO: 798 | Polypeptide encoded by SEQ ID NO: 797 | 30 aa |
| SEQ ID NO: 799 | HepC1a segment 197 | 90 nts |
| SEQ ID NO: 800 | Polypeptide encoded by SEQ ID NO: 799 | 30 aa |
| SEQ ID NO: 801 | HepC1a segment 198 | 90 nts |
| SEQ ID NO: 802 | Polypeptide encoded by SEQ ID NO: 801 | 30 aa |
| SEQ ID NO: 803 | HepCla segment 199 | 90 nts |
| SEQ ID NO: 804 | Polypeptide encoded by SEQ ID NO: 803 | 30 aa |
| SEQ ID NO: 805 | HepCla segment 200 | 90 nts |
| SEQ ID NO: 806 | Polypeptide encoded by SEQ ID NO: 805 | 30 aa |
| SEQ ID NO: 807 | HepC1a segment 201 | 45 nts |
| SEQ ID NO: 808 | Polypeptide encoded by SEQ ID NO: 807 | 15 aa |
| SEQ ID NO: 809 | HepC1a scrambled | 17955 nts |
| SEQ ID NO: 810 | Polypeptide encoded by SEQ ID NO: 809 | 5985 aa |
| SEQ ID NO: 811 | HepC Cassette A | 6065 nts |
| SEQ ID NO: 812 | Polypeptide encoded by SEQ ID NO: 811 | 2011 aa |
| SEQ ID NO: 813 | HepC Cassette B | 6069 nts |
| SEQ ID NO: 814 | Polypeptide encoded by SEQ ID NO: 813 | 2010 aa |

| STQUENCE ID NUMBER | SEQUENCE | LENGTH |
|-----------------------|---------------------------------------|----------|
| SEQ ID NO: 815 | HepC Cassette C | 6030 nts |
| SEQ ID NO: 816 | Polypeptide encoded by SEQ ID NO: 815 | 1997 aa |
| SEQ ID NO: 817 | gp100 consensus polypeptide | 661 aa |
| SEQ ID NO: 818 | MART consensus polypeptide | 118 aa |
| SEQ ID NO: 819 | TRP-1 consensus polypeptide | 248 aa |
| SEQ ID NO: 820 | Tyros consensus polypeptide | 529 aa |
| SEQ ID NO: 821 | TRP2 consensus polypeptide | 519 aa |
| SEQ ID NO: 822 | MC1R consensus polypeptide | 317 aa |
| SEQ ID NO: 823 | MUC1F consensus polypeptide | 125 aa |
| SEQ ID NO: 824 | MUC1R consensus polypeptide | 312 aa |
| SEQ ID NO: 825 | BAGE consensus polypeptide | 43 aa |
| SEQ ID NO: 826 | GAGE-1 consensus polypeptide | 138 aa |
| SEQ ID NO: 827 | gp100ln4 consensus polypeptide | 51 aa |
| SEQ ID NO: 828 | MAGE-1 consensus polypeptide | 309 aa |
| SEQ ID NO: 829 | MAGE-3 consensus polypeptide | 314 aa |
| SEQ ID NO: 830 | PRAME consensus polypeptide | 509 aa |
| SEQ ID NO: 831 | TRP2IN2 consensus polypeptide | 54 aa |
| SEQ ID NO: 832 | NYNSO1a consensus polypeptide | 180 aa |
| SEQ ID NO: 833 | NYNSO1b consensus polypeptide | 58 aa |
| SEQ ID NO: 834 | LAGE1 consensus polypeptide | 180 aa |
| SEQ ID NO: 835 | gp100 segment 1 | 90 nts |
| SEQ ID NO: 836 | Polypeptide encoded by SEQ ID NO: 835 | 30 aa |
| SEQ ID NO: 837 | gp100 segment 2 | 90 nts |
| SEQ ID NO: 838 | Polypeptide encoded by SEQ ID NO: 837 | 30 aa |

| SEQUENCE ID NUMBER | SEQUENCE | LENGTH |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 839 | gp100 segment 3 | 90 nts |
| SEQ ID NO: 840 | Polypeptide encoded by SEQ ID NO: 839 | 30 aa |
| SEQ ID NO: 841 | gp100 segment 4 | 90 nts |
| SEQ ID NO: 842 | Polypeptide encoded by SEQ ID NO: 841 | 30 aa |
| SEQ ID NO: 843 | gp100 segment 5 | 90 nts |
| SEQ ID NO: 844 | Polypeptide encoded by SEQ ID NO: 843 | 30 aa |
| SEQ ID NO: 845 | gp100 segment 6 | 90 nts |
| SEQ ID NO: 846 | Polypeptide encoded by SEQ ID NO: 845 | 30 aa |
| SEQ ID NO: 847 | gp100 segment 7 | 90 nts |
| SEQ ID NO: 848 | Polypeptide encoded by SEQ ID NO: 847 | 30 aa |
| SEQ ID NO: 849 | gp100 segment 8 | 90 nts |
| SEQ ID NO: 850 | Polypeptide encoded by SEQ ID NO: 849 | 30 aa |
| SEQ ID NO: 851 | gp100 segment 9 | 90 nts |
| SEQ ID NO: 852 | Polypeptide encoded by SEQ ID NO: 851 | 30 aa |
| SEQ ID NO: 853 | gp100 segment 10 | 90 nts |
| SEQ ID NO: 854 | Polypeptide encoded by SEQ ID NO: 853 | 30 aa |
| SEQ ID NO: 855 | gp100 segment 11 | 90 nts |
| SEQ ID NO: 856 | Polypeptide encoded by SEQ ID NO: 855 | 30 aa |
| SEQ ID NO: 857 | gp100 segment 12 | 90 nts |
| SEQ ID NO: 858 | Polypeptide encoded by SEQ ID NO: 857 | 30 aa |
| SEQ ID NO: 859 | gp100 segment 13 | 90 nts |
| SEQ ID NO: 860 | Polypeptide encoded by SEQ ID NO: 859 | 30 aa |
| SEQ ID NO: 861 | gp100 segment 14 | 90 nts |
| SEQ ID NO: 862 | Polypeptide encoded by SEQ ID NO: 861 | 30 aa |

| SEQUENCI ID MUMBER | SIGUINCI | LINGTH |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 863 | gp100 segment 15 | 90 nts |
| SEQ ID NO: 864 | Polypeptide encoded by SEQ ID NO: 863 | 30 aa |
| SEQ ID NO: 865 | gp100 segment 16 | 90 nts |
| SEQ ID NO: 866 | Polypeptide encoded by SEQ ID NO: 865 | 30 aa |
| SEQ ID NO: 867 | gp100 segment 17 | 90 nts |
| SEQ ID NO: 868 | Polypeptide encoded by SEQ ID NO: 867 | 30 aa |
| SEQ ID NO: 869 | gp100 segment 18 | 90 nts |
| SEQ ID NO: 870 | Polypeptide encoded by SEQ ID NO: 869 | 30 aa |
| SEQ ID NO: 871 | gp100 segment 19 | 90 nts |
| SEQ ID NO: 872 | Polypeptide encoded by SEQ ID NO: 871 | 30 aa |
| SEQ ID NO: 873 | gp100 segment 20 | 90 nts |
| SEQ ID NO: 874 | Polypeptide encoded by SEQ ID NO: 873 | 30 aa |
| SEQ ID NO: 875 | gp100 segment 21 | 90 nts |
| SEQ ID NO: 876 | Polypeptide encoded by SEQ ID NO: 875 | 30 aa |
| SEQ ID NO: 877 | gp100 segment 22 | 90 nts |
| SEQ ID NO: 878 | Polypeptide encoded by SEQ ID NO: 877 | 30 aa |
| SEQ ID NO: 879 | gp100 segment 23 | 90 nts |
| SEQ ID NO: 880 | Polypeptide encoded by SEQ ID NO: 879 | 30 aa |
| SEQ ID NO: 881 | gp100 segment 24 | 90 nts |
| SEQ ID NO: 882 | Polypeptide encoded by SEQ ID NO: 881 | 30 aa |
| SEQ ID NO: 883 | gp100 segment 25 | 90 nts |
| SEQ ID NO: 884 | Polypeptide encoded by SEQ ID NO: 883 | 30 aa |
| SEQ ID NO: 885 | gp100 segment 26 | 90 nts |
| SEQ ID NO: 886 | Polypeptide encoded by SEQ ID NO: 885 | 30 aa |

| NQUENCI D NUMBIR | SEQUENCE | LIENGTH |
|---------------------|---------------------------------------|---------|
| SEQ ID NO: 887 | gp100 segment 27 | 90 nts |
| SEQ ID NO: 888 | Polypeptide encoded by SEQ ID NO: 887 | 30 aa |
| SEQ ID NO: 889 | gp100 segment 28 | 90 nts |
| SEQ ID NO: 890 | Polypeptide encoded by SEQ ID NO: 889 | 30 aa |
| SEQ ID NO: 891 | gp100 segment 29 | 90 nts |
| SEQ ID NO: 892 | Polypeptide encoded by SEQ ID NO: 891 | 30 aa |
| SEQ ID NO: 893 | gp100 segment 30 | 90 nts |
| SEQ ID NO: 894 | Polypeptide encoded by SEQ ID NO: 893 | 30 aa |
| SEQ ID NO: 895 | gp100 segment 31 | 90 nts |
| SEQ ID NO: 896 | Polypeptide encoded by SEQ ID NO: 895 | 30 aa |
| SEQ ID NO: 897 | gp100 segment 32 | 90 nts |
| SEQ ID NO: 898 | Polypeptide encoded by SEQ ID NO: 897 | 30 aa |
| SEQ ID NO: 899 | gp100 segment 33 | 90 nts |
| SEQ ID NO: 900 | Polypeptide encoded by SEQ ID NO: 899 | 30 aa |
| SEQ ID NO: 901 | gp100 segment 34 | 90 nts |
| SEQ ID NO: 902 | Polypeptide encoded by SEQ ID NO: 901 | 30 aa |
| SEQ ID NO: 903 | gp100 segment 35 | 90 nts |
| SEQ ID NO: 904 | Polypeptide encoded by SEQ ID NO: 903 | 30 aa |
| SEQ ID NO: 905 | gp100 segment 36 | 90 nts |
| SEQ ID NO: 906 | Polypeptide encoded by SEQ ID NO: 905 | 30 aa |
| SEQ ID NO: 907 | gp100 segment 37 | 90 nts |
| SEQ ID NO: 908 | Polypeptide encoded by SEQ ID NO: 907 | 30 aa |
| SEQ ID NO: 909 | gp100 segment 38 | 90 nts |
| SEQ ID NO: 910 | Polypeptide encoded by SEQ ID NO: 909 | 30 aa |

| SEGLENCI ID: MUMBER | : SEQUENCE | LENGTH |
|------------------------|---------------------------------------|--------|
| SEQ ID NO: 911 | gp100 segment 39 | 90 nts |
| SEQ ID NO: 912 | Polypeptide encoded by SEQ ID NO: 911 | 30 aa |
| SEQ ID NO: 913 | gp100 segment 40 | 90 nts |
| SEQ ID NO: 914 | Polypeptide encoded by SEQ ID NO: 913 | 30 aa |
| SEQ ID NO: 915 | gp100 segment 41 | 90 nts |
| SEQ ID NO: 916 | Polypeptide encoded by SEQ ID NO: 915 | 30 aa |
| SEQ ID NO: 917 | gp100 segment 42 | 90 nts |
| SEQ ID NO: 918 | Polypeptide encoded by SEQ ID NO: 917 | 30 aa |
| SEQ ID NO: 919 | gp100 segment 43 | 90 nts |
| SEQ ID NO: 920 | Polypeptide encoded by SEQ ID NO: 919 | 30 aa |
| SEQ ID NO: 921 | gp100 segment 44 | 60nts |
| SEQ ID NO: 922 | Polypeptide encoded by SEQ ID NO: 921 | 20 aa |
| SEQ ID NO: 923 | MART segment 1 | 90 nts |
| SEQ ID NO: 924 | Polypeptide encoded by SEQ ID NO: 923 | 30 aa |
| SEQ ID NO: 925 | MART segment 2 | 90 nts |
| SEQ ID NO: 926 | Polypeptide encoded by SEQ ID NO: 925 | 30 aa |
| SEQ ID NO: 927 | MART segment 3 | 90 nts |
| SEQ ID NO: 928 | Polypeptide encoded by SEQ ID NO: 927 | 30 aa |
| SEQ ID NO: 929 | MART segment 4 | 90 nts |
| SEQ ID NO: 930 | Polypeptide encoded by SEQ ID NO: 929 | 30 aa |
| SEQ ID NO: 931 | MART segment 5 | 90 nts |
| SEQ ID NO: 932 | Polypeptide encoded by SEQ ID NO: 931 | 30 aa |
| SEQ ID NO: 933 | MART segment 6 | 90 nts |
| SEQ ID NO: 934 | Polypeptide encoded by SEQ ID NO: 933 | 30 aa |

| SZQVINCI D MUVBIR | EQUE CI | LENGTH |
|----------------------|---------------------------------------|--------|
| SEQ ID NO: 935 | MART segment 7 | 90 nts |
| SEQ ID NO: 936 | Polypeptide encoded by SEQ ID NO: 935 | 30 aa |
| SEQ ID NO: 937 | MART segment 8 | 51 nts |
| SEQ ID NO: 938 | Polypeptide encoded by SEQ ID NO: 937 | 17 aa |
| SEQ ID NO: 939 | trp-1 segment 1 | 90 nts |
| SEQ ID NO: 940 | Polypeptide encoded by SEQ ID NO: 939 | 30 aa |
| SEQ ID NO: 941 | trp-1 segment 2 | 90 nts |
| SEQ ID NO: 942 | Polypeptide encoded by SEQ ID NO: 941 | 30 aa |
| SEQ ID NO: 943 | trp-1 segment 3 | 90 nts |
| SEQ ID NO: 944 | Polypeptide encoded by SEQ ID NO: 943 | 30 aa |
| SEQ ID NO: 945 | trp-1 segment 4 | 90 nts |
| SEQ ID NO: 946 | Polypeptide encoded by SEQ ID NO: 945 | 30 aa |
| SEQ ID NO: 947 | trp-1 segment 5 | 90 nts |
| SEQ ID NO: 948 | Polypeptide encoded by SEQ ID NO: 947 | 30 aa |
| SEQ ID NO: 949 | trp-1 segment 6 | 90 nts |
| SEQ ID NO: 950 | Polypeptide encoded by SEQ ID NO: 949 | 30 aa |
| SEQ ID NO: 951 | trp-1 segment 7 | 90 nts |
| SEQ ID NO: 952 | Polypeptide encoded by SEQ ID NO: 951 | 30 aa |
| SEQ ID NO: 953 | trp-1 segment 8 | 90 nts |
| SEQ ID NO: 954 | Polypeptide encoded by SEQ ID NO: 953 | 30 aa |
| SEQ ID NO: 955 | trp-1 segment 9 | 90 nts |
| SEQ ID NO: 956 | Polypeptide encoded by SEQ ID NO: 955 | 30 aa |
| SEQ ID NO: 957 | trp-1 segment 10 | 90 nts |
| SEQ ID NO: 958 | Polypeptide encoded by SEQ ID NO: 957 | 30 aa |

| MIQUINCE ID NUMBER | MOUTING | Lingth |
|-----------------------|---------------------------------------|--------|
| SEQ ID NO: 959 | trp-1 segment 11 | 90 nts |
| SEQ ID NO: 960 | Polypeptide encoded by SEQ ID NO: 959 | 30 aa |
| SEQ ID NO: 961 | trp-1 segment 12 | 90 nts |
| SEQ ID NO: 962 | Polypeptide encoded by SEQ ID NO: 961 | 30 aa |
| SEQ ID NO: 963 | trp-1 segment 13 | 90 nts |
| SEQ ID NO: 964 | Polypeptide encoded by SEQ ID NO: 963 | 30 aa |
| SEQ ID NO: 965 | trp-1 segment 14 | 90 nts |
| SEQ ID NO: 966 | Polypeptide encoded by SEQ ID NO: 965 | 30 aa |
| SEQ ID NO: 967 | trp-1 segment 15 | 90 nts |
| SEQ ID NO: 968 | Polypeptide encoded by SEQ ID NO: 967 | 30 aa |
| SEQ ID NO: 969 | trp-1 segment 16 | 81 nts |
| SEQ ID NO: 970 | Polypeptide encoded by SEQ ID NO: 969 | 27 aa |
| SEQ ID NO: 971 | tyros segment 1 | 90 nts |
| SEQ ID NO: 972 | Polypeptide encoded by SEQ ID NO: 971 | 30 aa |
| SEQ ID NO: 973 | tyros segment 2 | 90 nts |
| SEQ ID NO: 974 | Polypeptide encoded by SEQ ID NO: 973 | 30 aa |
| SEQ ID NO: 975 | tyros segment 3 | 90 nts |
| SEQ ID NO: 976 | Polypeptide encoded by SEQ ID NO: 975 | 30 aa |
| SEQ ID NO: 977 | tyros segment 4 | 90 nts |
| SEQ ID NO: 978 | Polypeptide encoded by SEQ ID NO: 977 | 30 aa |
| SEQ ID NO: 979 | tyros segment 5 | 90 nts |
| SEQ ID NO: 980 | Polypeptide encoded by SEQ ID NO: 979 | 30 aa |
| SEQ ID NO: 981 | tyros segment 6 | 90 nts |
| SEQ ID NO: 982 | Polypeptide encoded by SEQ ID NO: 981 | 30 aa |

| SEQUENCE ID NUMBER | SEQUENCE | LENCTH |
|-----------------------|--|--------|
| SEQ ID NO: 983 | tyros segment 7 | 90 nts |
| SEQ ID NO: 984 | Polypeptide encoded by SEQ ID NO: 983 | 30 aa |
| SEQ ID NO: 985 | tyros segment 8 | 90 nts |
| SEQ ID NO: 986 | Polypeptide encoded by SEQ ID NO: 985 | 30 aa |
| SEQ ID NO: 987 | tyros segment 9 | 90 nts |
| SEQ ID NO: 988 | Polypeptide encoded by SEQ ID NO: 987 | 30 aa |
| SEQ ID NO: 989 | tyros segment 10 | 90 nts |
| SEQ ID NO: 990 . | Polypeptide encoded by SEQ ID NO: 989 | 30 aa |
| SEQ ID NO: 991 | tyros segment 11 | 90 nts |
| SEQ ID NO: 992 | Polypeptide encoded by SEQ ID NO: 991 | 30 aa |
| SEQ ID NO: 993 | tyros segment 12 | 90 nts |
| SEQ ID NO: 994 | Polypeptide encoded by SEQ ID NO: 993 | 30 aa |
| SEQ ID NO: 995 | tyros segment 13 | 90 nts |
| SEQ ID NO: 996 | Polypeptide encoded by SEQ ID NO: 995 | 30 aa |
| SEQ ID NO: 997 | tyros segment 14 | 90 nts |
| SEQ ID NO: 998 | Polypeptide encoded by SEQ ID NO: 997 | 30 aa |
| SEQ ID NO: 999 | tyros segment 15 | 90 nts |
| SEQ ID NO: 1000 | Polypeptide encoded by SEQ ID NO: 999 | 30 aa |
| SEQ ID NO: 1001 | tyros segment 16 | 90 nts |
| SEQ ID NO: 1002 | Polypeptide encoded by SEQ ID NO: 1001 | 30 aa |
| SEQ ID NO: 1003 | tyros segment 17 | 90 nts |
| SEQ ID NO: 1004 | Polypeptide encoded by SEQ ID NO: 1003 | 30 aa |
| SEQ ID NO: 1005 | tyros segment 18 | 90 nts |
| SEQ ID NO: 1006 | Polypeptide encoded by SEQ ID NO: 1005 | 30 aa |

| SECUTACE 1D AUMBER | LIQUENCE | UENGTH |
|------------------------|--|--------|
| SEQ ID NO: 1007 | tyros segment 19 | 90 nts |
| SEQ ID NO: 1008 | Polypeptide encoded by SEQ ID NO: 1007 | 30 aa |
| SEQ ID NO: 1009 | tyros segment 20 | 90 nts |
| SEQ ID NO: 1010 | Polypeptide encoded by SEQ ID NO: 1009 | 30 aa |
| SEQ ID NO: 1011 | tyros segment 21 | 90 nts |
| SEQ ID NO: 1012 | Polypeptide encoded by SEQ ID NO: 1011 | 30 aa |
| SEQ ID NO: 1013 | tyros segment 22 | 90 nts |
| SEQ ID NO: 1014 | Polypeptide encoded by SEQ ID NO: 1013 | 30 aa |
| SEQ ID NO: 1015 | tyros segment 23 | 90 nts |
| SEQ ID NO: 1016 | Polypeptide encoded by SEQ ID NO: 1015 | 30 aa |
| SEQ ID NO: 1017 | tyros segment 24 | 90 nts |
| SEQ ID NO: 1018 | Polypeptide encoded by SEQ ID NO: 1017 | 30 aa |
| SEQ ID NO: 1019 | tyros segment 25 | 90 nts |
| SEQ ID NO: 1020 | Polypeptide encoded by SEQ ID NO: 1019 | 30 aa |
| SEQ ID NO: 1021 | tyros segment 26 | 90 nts |
| SEQ ID NO: 1022 | Polypeptide encoded by SEQ ID NO: 1021 | 30 aa |
| SEQ ID NO: 1023 | tyros segment 27 | 90 nts |
| SEQ ID NO: 1024 | Polypeptide encoded by SEQ ID NO: 1023 | 30 aa |
| SEQ ID NO: 1025 | tyros segment 28 | 90 nts |
| SEQ ID NO: 1026 | Polypeptide encoded by SEQ ID NO: 1025 | 30 aa |
| SEQ ID NO: 1027 | tyros segment 29 | 90 nts |
| SEQ ID NO: 1028 | Polypeptide encoded by SEQ ID NO: 1027 | 30 aa |
| SEQ ID NO: 1029 | tyros segment 30 | 90 nts |
| SEQ ID NO: 1030 | Polypeptide encoded by SEQ ID NO: 1029 | 30 aa |

| MOUINCE ID NUMBER | SEQUENCE | LINGTH |
|----------------------|--|----------|
| SEQ ID NO: 1031 | tyros segment 31 | 90 nts |
| SEQ ID NO: 1032 | Polypeptide encoded by SEQ ID NO: 1031 | 30 aa |
| SEQ ID NO: 1033 | tyros segment 32 | 90 nts |
| SEQ ID NO: 1034 | Polypeptide encoded by SEQ ID NO: 1033 | 30 aa |
| SEQ ID NO: 1035 | tyros segment 33 | 90 nts |
| SEQ ID NO: 1036 | Polypeptide encoded by SEQ ID NO: 1035 | 30 aa |
| SEQ ID NO: 1037 | tyros segment 34 | 90 nts |
| SEQ ID NO: 1038 | Polypeptide encoded by SEQ ID NO: 1037 | 30 aa |
| SEQ ID NO: 1039 | tyros segment 35 | 69 nts |
| SEQ ID NO: 1040 | Polypeptide encoded by SEQ ID NO: 1039 | 23 aa |
| SEQ ID NO: 1041 | trp2 segment 1 | 90 nts |
| SEQ ID NO: 1042 | Polypeptide encoded by SEQ ID NO: 1041 | 30 aa |
| SEQ ID NO: 1043. | trp2 segment 2 | 90 nts |
| SEQ ID NO: 1044 | Polypeptide encoded by SEQ ID NO: 1043 | 30 aa |
| SEQ ID NO: 1045 | trp2 segment 3 | 90 nts |
| SEQ ID NO: 1046 | Polypeptide encoded by SEQ ID NO: 1045 | 30 aa |
| SEQ ID NO: 1047 | trp2 segment 4 | 90 nts |
| SEQ ID NO: 1048 | Polypeptide encoded by SEQ ID NO: 1047 | 30 aa |
| SEQ ID NO: 1049 | trp2 segment 5 | 90 nts _ |
| SEQ ID NO: 1050 | Polypeptide encoded by SEQ ID NO: 1049 | 30 aa |
| SEQ ID NO: 1051 | trp2 segment 6 | .90 nts |
| SEQ ID NO: 1052 | Polypeptide encoded by SEQ ID NO: 1051 | 30 aa |
| SEQ ID NO: 1053 | trp2 segment 7 | 90 nts |
| ·SEQ ID NO: 1054 | Polypeptide encoded by SEQ ID NO: 1053 | 30 aa |

| SEQUENCE EL NUMBER | SEQUENCE | LENGTH |
|------------------------|--|--------|
| SEQ ID NO: 1055 | trp2 segment 8 | 90 nts |
| SEQ ID NO: 1056 | Polypeptide encoded by SEQ ID NO: 1055 | 30 aa |
| SEQ ID NO: 1057 | trp2 segment 9 | 90 nts |
| SEQ ID NO: 1058 | Polypeptide encoded by SEQ ID NO: 1057 | 30 aa |
| SEQ ID NO: 1059 | trp2 segment 10 | 90 nts |
| SEQ ID NO: 1060 | Polypeptide encoded by SEQ ID NO: 1059 | 30 aa |
| SEQ ID NO: 1061 | trp2 segment 11 | 90 nts |
| SEQ ID NO: 1062 | Polypeptide encoded by SEQ ID NO: 1061 | 30 aa |
| SEQ ID NO: 1063 | trp2 segment 12 | 90 nts |
| SEQ ID NO: 1064 | Polypeptide encoded by SEQ ID NO: 1063 | 30 aa |
| SEQ ID NO: 1065 | trp2 segment 13 | 90 nts |
| SEQ ID NO: 1066 | Polypeptide encoded by SEQ ID NO: 1065 | 30 aa |
| SEQ ID NO: 1067 | trp2 segment 14 | 90 nts |
| SEQ ID NO: 1068 | Polypeptide encoded by SEQ ID NO: 1067 | 30 aa |
| SEQ ID NO: 1069 | trp2 segment 15 | 90 nts |
| SEQ ID NO: 1070 | Polypeptide encoded by SEQ ID NO: 1069 | 30 aa |
| SEQ ID NO: 1071 | trp2 segment 16 | 90 nts |
| SEQ ID NO: 1072 | Polypeptide encoded by SEQ ID NO: 1071 | 30 aa |
| SEQ ID NO: 1073 | trp2 segment 17 | 90 nts |
| SEQ ID NO: 1074 | Polypeptide encoded by SEQ ID NO: 1073 | 30 aa |
| SEQ ID NO: 1075 | trp2 segment 18 | 90 nts |
| SEQ ID NO: 1076 | Polypeptide encoded by SEQ ID NO: 1075 | 30 aa |
| SEQ ID NO: 1077 | trp2 segment 19 | 90 nts |
| SEQ ID NO: 1078 | Polypeptide encoded by SEQ ID NO: 1077 | 30 aa |

| SIQUENCI ID NUMBER | SEQUENCE | LENGTH |
|-----------------------|--|---------|
| SEQ ID NO: 1079 | trp2 segment 20 | 90 nts |
| SEQ ID NO: 1080 | Polypeptide encoded by SEQ ID NO: 1079 | 30 aa 、 |
| SEQ ID NO: 1081 | trp2 segment 21 | 90 nts |
| SEQ ID NO: 1082 | Polypeptide encoded by SEQ ID NO: 1081 | 30 aa |
| SEQ ID NO: 1083 | trp2 segment 22 | 90 nts |
| SEQ ID NO: 1084 | Polypeptide encoded by SEQ ID NO: 1083 | 30 aa |
| SEQ ID NO: 1085 | trp2 segment 23 | 90 nts |
| SEQ ID NO: 1086 | Polypeptide encoded by SEQ ID NO: 1085 | 30 aa |
| SEQ ID NO: 1087 | trp2 segment 24 | 90 nts |
| SEQ ID NO: 1088 | Polypeptide encoded by SEQ ID NO: 1087 | 30 aa |
| SEQ ID NO: 1089 | trp2 segment 25 | 90 nts |
| SEQ ID NO: 1090 | Polypeptide encoded by SEQ ID NO: 1089 | 30 aa . |
| SEQ ID NO: 1091 | trp2 segment 26 | 90 nts |
| SEQ ID NO: 1092 | Polypeptide encoded by SEQ ID NO: 1091 | 30 aa |
| SEQ ID NO: 1093 | trp2 segment 27 | 90 nts |
| SEQ ID NO: 1094 | Polypeptide encoded by SEQ ID NO: 1093 | 30 aa |
| SEQ ID NO: 1095 | trp2 segment 28 | 90 nts |
| SEQ ID NO: 1096 | Polypeptide encoded by SEQ ID NO: 1095 | 30 aa |
| SEQ ID NO: 1097 | trp2 segment 29 | 90 nts |
| SEQ ID NO: 1098 | Polypeptide encoded by SEQ ID NO: 1097 | 30 aa |
| SEQ ID NO: 1099 | trp2 segment 30 | 90 nts |
| SEQ ID NO: 1100 | Polypeptide encoded by SEQ ID NO: 1099 | 30 aa |
| SEQ ID NO: 1101 | trp2 segment 31 | 90 nts |
| SEQ ID NO: 1102 | Polypeptide encoded by SEQ ID NO: 1101 | 30 aa |

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| SIQUENCI ID MUNBER | MQUEVCI | LENGTH |
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| SEQ ID NO: 1103 | trp2 segment 32 | 90 nts |
| SEQ ID NO: 1104 | Polypeptide encoded by SEQ ID NO: 1103 | 30 aa |
| SEQ ID NO: 1105 | trp2 segment 33 | 90 nts |
| SEQ ID NO: 1106 | Polypeptide encoded by SEQ ID NO: 1105 | 30 aa |
| SEQ ID NO: 1107 | trp2 segment 34 | 84 nts |
| SEQ ID NO: 1108 | Polypeptide encoded by SEQ ID NO: 1107 | 28 aa |
| SEQ ID NO: 1109 | MC1R segment 1 | 90 nts |
| SEQ ID NO: 1110 | Polypeptide encoded by SEQ ID NO: 1109 | 30 aa |
| SEQ ID NO: 1111 | MC1R segment 2 | 90 nts |
| SEQ ID NO: 1112 | Polypeptide encoded by SEQ ID NO: 1111 | 30 aa |
| SEQ ID NO: 1113 | MC1R segment 3 | 90 nts |
| SEQ ID NO: 1114 | Polypeptide encoded by SEQ ID NO: 1113 | 30 aa |
| SEQ ID NO: 1115 | MC1R segment 4 | 90 nts |
| SEQ ID NO: 1116 | Polypeptide encoded by SEQ ID NO: 1115 | 30 aa |
| SEQ ID NO: 1117 | MC1R segment 5 | 90 nts |
| SEQ ID NO: 1118 | Polypeptide encoded by SEQ ID NO: 1117 | 30 aa |
| SEQ ID NO: 1119 | MC1R segment 6 | 90 nts |
| SEQ ID NO: 1120 | Polypeptide encoded by SEQ ID NO: 1119 | 30 aa |
| SEQ ID NO: 1121 | MC1R segment 7 | 90 nts |
| SEQ ID NO: 1122 | Polypeptide encoded by SEQ ID NO: 1121 | 30 aa |
| SEQ ID NO: 1123 | MC1R segment 8 | 90 nts |
| SEQ ID NO: 1124 | Polypeptide encoded by SEQ ID NO: 1123 | 30 aa |
| SEQ ID NO: 1125 | MC1R segment 9 | 90 nts |
| SEQ ID NO: 1126 | Polypeptide encoded by SEQ ID NO: 1125 | 30 aa |

| SEQUENCE ID NUMBER | sequence | LINGTH |
|-----------------------|--|--------|
| SEQ ID NO: 1127 | MC1R segment 10 | 90 nts |
| SEQ ID NO: 1128 | Polypeptide encoded by SEQ ID NO: 1127 | 30 aa |
| SEQ ID NO: 1129 | MC1R segment 11 | 90 nts |
| SEQ ID NO: 1130 | Polypeptide encoded by SEQ ID NO: 1129 | 30 aa |
| SEQ ID NO: 1131 | MC1R segment 12 | 90 nts |
| SEQ ID NO: 1132 | Polypeptide encoded by SEQ ID NO: 1131 | 30 aa |
| SEQ ID NO: 1133 | MC1R segment 13 | 90 nts |
| SEQ ID NO: 1134 | Polypeptide encoded by SEQ ID NO: 1133 | 30 aa |
| SEQ ID NO: 1135 | MC1R segment 14 | 90 nts |
| SEQ ID NO: 1136 | Polypeptide encoded by SEQ ID NO: 1135 | 30 aa |
| SEQ ID NO: 1137 | MC1R segment 15 | 90 nts |
| SEQ ID NO: 1138 | Polypeptide encoded by SEQ ID NO: 1137 | 30 aa |
| SEQ ID NO: 1139 | MC1R segment 16 | 90 nts |
| SEQ ID NO: 1140 | Polypeptide encoded by SEQ ID NO: 1139 | 30 aa |
| SEQ ID NO: 1141 | MC1R segment 17 | 90 nts |
| SEQ ID NO: 1142 | Polypeptide encoded by SEQ ID NO: 1141 | 30 aa |
| SEQ ID NO: 1143 | MC1R segment 18 | 90 nts |
| SEQ ID NO: 1144 | Polypeptide encoded by SEQ ID NO: 1143 | 30 aa |
| SEQ ID NO: 1145 | MC1R segment 19 | 90 nts |
| SEQ ID NO: 1146 | Polypeptide encoded by SEQ ID NO: 1145 | 30 aa |
| SEQ ID NO: 1147 | MC1R segment 20 | 90 nts |
| SEQ ID NO: 1148 | Polypeptide encoded by SEQ ID NO: 1147 | 30 aa |
| SEQ ID NO: 1149 | MC1R segment 21 | 63 nts |
| SEQ ID NO: 1150 | Polypeptide encoded by SEQ ID NO: 1149 | 21 aa |

| MOUENCE DO | SECULENCE. | 1.EMGTH |
|-----------------|--|---------|
| NUMBER | යපැති දැනා ගුලක | |
| SEQ ID NO: 1151 | MUC1F segment 1 | 90 nts |
| SEQ ID NO: 1152 | Polypeptide encoded by SEQ ID NO: 1151 | 30 aa |
| SEQ ID NO: 1153 | MUC1F segment 2 | 90 nts |
| SEQ ID NO: 1154 | Polypeptide encoded by SEQ ID NO: 1153 | 30 aa |
| SEQ ID NO: 1155 | MUC1F segment 3 | 90 nts |
| SEQ ID NO: 1156 | Polypeptide encoded by SEQ ID NO: 1155 | 30 aa |
| SEQ ID NO: 1157 | MUC1F segment 4 | 90 nts |
| SEQ ID NO: 1158 | Polypeptide encoded by SEQ ID NO: 1157 | 30 aa |
| SEQ ID NO: 1159 | MUC1F segment 5 | 90 nts |
| SEQ ID NO: 1160 | Polypeptide encoded by SEQ ID NO: 1159 | 30 aa |
| SEQ ID NO: 1161 | MUC1F segment 6 | 90 nts |
| SEQ ID NO: 1162 | Polypeptide encoded by SEQ ID NO: 1161 | 30 aa |
| SEQ ID NO: 1163 | MUC1F segment 7 | 90 nts |
| SEQ ID NO: 1164 | Polypeptide encoded by SEQ ID NO: 1163 | 30 aa |
| SEQ ID NO: 1165 | MUC1F segment 8 | 72 nts |
| SEQ ID NO: 1166 | Polypeptide encoded by SEQ ID NO: 1165 | 24 aa |
| SEQ ID NO: 1167 | MUC1R segment 1 | 90 nts |
| SEQ ID NO: 1168 | Polypeptide encoded by SEQ ID NO: 1167 | 30 aa |
| SEQ ID NO: 1169 | MUC1R segment 2 | 90 nts |
| SEQ ID NO: 1170 | Polypeptide encoded by SEQ ID NO: 1169 | 30 aa |
| SEQ ID NO: 1171 | MUC1R segment 3 | 90 nts |
| SEQ ID NO: 1172 | Polypeptide encoded by SEQ ID NO: 1171 | 30 aa |
| SEQ ID NO: 1173 | MUC1R segment 4 | 90 nts |
| SEQ ID NO: 1174 | Polypeptide encoded by SEQ ID NO: 1173 | 30 aa |

| SIQUENCI ID NUIBLR | SEQUENCE | LENGTH |
|-----------------------|--|--------|
| SEQ ID NO: 1175 | MUC1R segment 5 | 90 nts |
| SEQ ID NO: 1176 | Polypeptide encoded by SEQ ID NO: 1175 | 30 aa |
| SEQ ID NO: 1177 | MUC1R segment 6 | 90 nts |
| SEQ ID NO: 1178 | Polypeptide encoded by SEQ ID NO: 1177 | 30 aa |
| SEQ ID NO: 1179 | MUC1R segment 7 | 90 nts |
| SEQ ID NO: 1180 | Polypeptide encoded by SEQ ID NO: 1179 | 30 aa |
| SEQ ID NO: 1181 | MUC1R segment 8 | 90 nts |
| SEQ ID NO: 1182 | Polypeptide encoded by SEQ ID NO: 1181 | 30 aa |
| SEQ ID NO: 1183 | MUC1R segment 9 | 90 nts |
| SEQ ID NO: 1184 | Polypeptide encoded by SEQ ID NO: 1183 | 30 aa |
| SEQ ID NO: 1185 | MUC1R segment 10 | 90 nts |
| SEQ ID NO: 1186 | Polypeptide encoded by SEQ ID NO: 1185 | 30 aa |
| SEQ ID NO: 1187 | MUC1R segment 11 | 90 nts |
| SEQ ID NO: 1188 | Polypeptide encoded by SEQ ID NO: 1187 | 30 aa |
| SEQ ID NO: 1189 | MUC1R segment 12 | 90 nts |
| SEQ ID NO: 1190 | Polypeptide encoded by SEQ ID NO: 1189 | 30 aa |
| SEQ ID NO: 1191 | MUC1R segment 13 | 90 nts |
| SEQ ID NO: 1192 | Polypeptide encoded by SEQ ID NO: 1191 | 30 aa |
| SEQ ID NO: 1193 | MUC1R segment 14 | 90 nts |
| SEQ ID NO: 1194 | Polypeptide encoded by SEQ ID NO: 1193 | 30 aa |
| SEQ ID NO: 1195 | MUC1R segment 15 | 90 nts |
| SEQ ID NO: 1196 | Polypeptide encoded by SEQ ID NO: 1195 | 30 aa |
| SEQ ID NO: 1197 | MUC1R segment 16 | 90 nts |
| SEQ ID NO: 1198 | Polypeptide encoded by SEQ ID NO: 1197 | 30 aa |

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| SEQUENCE OD NUMBER | SEGIENCE | LENGTH |
|-----------------------|--|-----------|
| SEQ ID NO: 1199 | MUC1R segment 17 | 90 nts |
| SEQ ID NO: 1200 | Polypeptide encoded by SEQ ID NO: 1199 | 30 aa |
| SEQ ID NO: 1201 | MUC1R segment 18 | 90 nts |
| SEQ ID NO: 1202 | Polypeptide encoded by SEQ ID NO: 1201 | 30 aa |
| SEQ ID NO: 1203 | MUC1R segment 19 | 90 nts |
| SEQ ID NO: 1204 | Polypeptide encoded by SEQ ID NO: 1203 | 30 aa |
| SEQ ID NO: 1205 | MUC1R segment 20 | 90 nts |
| SEQ ID NO: 1206 | Polypeptide encoded by SEQ ID NO: 1205 | 30 aa |
| SEQ ID NO: 1207 | MUC1R segment 21 | 48 nts |
| SEQ ID NO: 1208 | Polypeptide encoded by SEQ ID NO: 1207 | 16 aa |
| SEQ ID NO: 1209 | Differentiation Savine | 16638 nts |
| SEQ ID NO: 1210 | Polypeptide encoded by SEQ ID NO: 1209 | 5546 aa |
| SEQ ID NO: 1211 | BAGE segment 1 | 90 nts |
| SEQ ID NO: 1212 | Polypeptide encoded by SEQ ID NO: 1211 | 30 aa |
| SEQ ID NO: 1213 | BAGE segment 2 | 90 nts |
| SEQ ID NO: 1214 | Polypeptide encoded by SEQ ID NO: 1213 | 30 aa |
| SEQ ID NO: 1215 | BAGE segment 3 | 51 nts |
| SEQ ID NO: 1216 | Polypeptide encoded by SEQ ID NO: 1215 | 17 aa |
| SEQ ID NO: 1217 | GAGE-1 segment 1 | 90 nts |
| SEQ ID NO: 1218 | Polypeptide encoded by SEQ ID NO: 1217 | 30 aa |
| SEQ ID NO: 1219 | GAGE-1 segment 2 | 90 nts |
| SEQ ID NO: 1220 | Polypeptide encoded by SEQ ID NO: 1219 | 30 aa |
| SEQ ID NO: 1221 | GAGE-1 segment 3 | 90 nts |
| SEQ ID NO: 1222 | Polypeptide encoded by SEQ ID NO: 1221 | 30 aa |

| SEQUENCE D | SEQUENCE | LENGTH |
|------------------------|--|--------|
| MUMBER | | |
| SEQ ID NO: 1223 | GAGE-1 segment 4 | 90 nts |
| SEQ ID NO: 1224 | Polypeptide encoded by SEQ ID NO: 1223 | 30 aa |
| SEQ ID NO: 1225 | GAGE-1 segment 5 | 90 nts |
| SEQ ID NO: 1226 | Polypeptide encoded by SEQ ID NO: 1225 | 30 aa |
| SEQ ID NO: 1227 | GAGE-1 segment 6 | 90 nts |
| SEQ ID NO: 1228 | Polypeptide encoded by SEQ ID NO: 1227 | 30 aa |
| SEQ ID NO: 1229 | GAGE-1 segment 7 | 90 nts |
| SEQ ID NO: 1230 | Polypeptide encoded by SEQ ID NO: 1229 | 30 aa |
| SEQ ID NO: 1231 | GAGE-1 segment 8 | 90 nts |
| SEQ ID NO: 1232 | Polypeptide encoded by SEQ ID NO: 1231 | 30 aa |
| SEQ ID NO: 1233 | GAGE-1 segment 9 | 66 nts |
| SEQ ID NO: 1234 | Polypeptide encoded by SEQ ID NO: 1233 | 22 aa |
| SEQ ID NO: 1235 | gp100ln4 segment 1 | 90 nts |
| SEQ ID NO: 1236 | Polypeptide encoded by SEQ ID NO: 1235 | 30 aa |
| SEQ ID NO: 1237 | gp100ln4 segment 2 | 90 nts |
| SEQ ID NO: 1238 | Polypeptide encoded by SEQ ID NO: 1237 | 30 aa |
| SEQ ID NO: 1239 | gp100ln4 segment 3 | 75 nts |
| SEQ ID NO: 1240 | Polypeptide encoded by SEQ ID NO: 1239 | 25 aa |
| SEQ ID NO: 1241 | MAGE-1 segment 1 | 90 nts |
| SEQ ID NO: 1242 | Polypeptide encoded by SEQ ID NO: 1241 | 30 aa |
| SEQ ID NO: 1243 | MAGE-1 segment 2 | 90 nts |
| SEQ ID NO: 1244 | Polypeptide encoded by SEQ ID NO: 1243 | 30 aa |
| SEQ ID NO: 1245 | MAGE-1 segment 3 | 90 nts |
| SEQ ID NO: 1246 | Polypeptide encoded by SEQ ID NO: 1245 | 30 aa |

| SEQUENCE ID NUMBER | Siguenci | LINGTH |
|-----------------------|--|--------|
| SEQ ID NO: 1247 | MAGE-1 segment 4 | 90 nts |
| SEQ ID NO: 1248 | Polypeptide encoded by SEQ ID NO: 1247 | 30 aa |
| SEQ ID NO: 1249 | MAGE-1 segment 5 | 90 nts |
| SEQ ID NO: 1250 | Polypeptide encoded by SEQ ID NO: 1249 | 30 aa |
| SEQ ID NO: 1251 | MAGE-1 segment 6 | 90 nts |
| SEQ ID NO: 1252 | Polypeptide encoded by SEQ ID NO: 1251 | 30 aa |
| SEQ ID NO: 1253 | MAGE-1 segment 7 | 90 nts |
| SEQ ID NO: 1254 | Polypeptide encoded by SEQ ID NO: 1253 | 30 aa |
| SEQ ID NO: 1255 | MAGE-1 segment 8 | 90 nts |
| SEQ ID NO: 1256 | Polypeptide encoded by SEQ ID NO: 1255 | 30 aa |
| SEQ ID NO: 1257 | .MAGE-1 segment 9 | 90 nts |
| SEQ ID NO: 1258 | Polypeptide encoded by SEQ ID NO: 1257 | 30 aa |
| SEQ ID NO: 1259 | MAGE-1 segment 10 | 90 nts |
| SEQ ID NO: 1260 | Polypeptide encoded by SEQ ID NO: 1259 | 30 aa |
| SEQ ID NO: 1261 | MAGE-1 segment 11 | 90 nts |
| SEQ ID NO: 1262 | Polypeptide encoded by SEQ ID NO: 1261 | 30 aa |
| SEQ ID NO: 1263 | MAGE-1 segment 12 | 90 nts |
| SEQ ID NO: 1264 | Polypeptide encoded by SEQ ID NO: 1263 | 30 aa |
| SEQ ID NO: 1265 | MAGE-1 segment 13 | 90 nts |
| SEQ ID NO: 1266 | Polypeptide encoded by SEQ ID NO: 1265 | 30 aa |
| SEQ ID NO: 1267 | MAGE-1 segment 14. | 90 nts |
| SEQ ID NO: 1268 | Polypeptide encoded by SEQ ID NO: 1267 | 30 aa |
| SEQ ID NO: 1269 | MAGE-1 segment 15 | 90 nts |
| SEQ ID NO: 1270 | Polypeptide encoded by SEQ ID NO: 1269 | 30 aa |

| DEQUENCS ID NUMBER | SIQUENCE | LENGTH |
|-----------------------|--|--------|
| SEQ ID NO: 1271 | MAGE-1 segment 16 | 90 nts |
| SEQ ID NO: 1272 | Polypeptide encoded by SEQ ID NO: 1271 | 30 aa |
| SEQ ID NO: 1273 | MAGE-1 segment 17 | 90 nts |
| SEQ ID NO: 1274 | Polypeptide encoded by SEQ ID NO: 1273 | 30 aa |
| SEQ ID NO: 1275 | MAGE-1 segment 18 | 90 nts |
| SEQ ID NO: 1276 | Polypeptide encoded by SEQ ID NO: 1275 | 30 aa |
| SEQ ID NO: 1277 | MAGE-1 segment 19 | 90 nts |
| SEQ ID NO: 1278 | Polypeptide encoded by SEQ ID NO: 1277 | 30 aa |
| SEQ ID NO: 1279 | MAGE-1 segment 20 | 84 nts |
| SEQ ID NO: 1280 | Polypeptide encoded by SEQ ID NO: 1279 | 28 aa |
| SEQ ID NO: 1281 | MAGE-3 segment 1 | 90 nts |
| SEQ ID NO: 1282 | Polypeptide encoded by SEQ ID NO: 1281 | 30 aa |
| SEQ ID NO: 1283 | MAGE-3 segment 2 | 90 nts |
| SEQ ID NO: 1284 | Polypeptide encoded by SEQ ID NO: 1283 | 30 aa |
| SEQ ID NO: 1285 | MAGE-3 segment 3 | 90 nts |
| SEQ ID NO: 1286 | Polypeptide encoded by SEQ ID NO: 1285 | 30 aa |
| SEQ ID NO: 1287 | MAGE-3 segment 4 | 90 nts |
| SEQ ID NO: 1288 | Polypeptide encoded by SEQ ID NO: 1287 | 30 aa |
| SEQ ID NO: 1289 | MAGE-3 segment 5 | 90 nts |
| SEQ ID NO: 1290 | Polypeptide encoded by SEQ ID NO: 1289 | 30 aa |
| SEQ ID NO: 1291 | MAGE-3 segment 6 | 90 nts |
| SEQ ID NO: 1292 | Polypeptide encoded by SEQ ID NO: 1291 | 30 aa |
| SEQ ID NO: 1293 | MAGE-3 segment 7 | 90 nts |
| SEQ ID NO: 1294 | Polypeptide encoded by SEQ ID NO: 1293 | 30 aa |

| TEQUENCI ID NUMBER | SIQUENCE | LENGTH |
|-----------------------|--|--------|
| SEQ ID NO: 1295 | MAGE-3 segment 8 | 90 nts |
| SEQ ID NO: 1296 | Polypeptide encoded by SEQ ID NO: 1295 | 30 aa |
| SEQ ID NO: 1297 | MAGE-3 segment 9 | 90 nts |
| SEQ ID NO: 1298 | Polypeptide encoded by SEQ ID NO: 1297 | 30 aa |
| SEQ ID NO: 1299 | MAGE-3 segment 10 | 90 nts |
| SEQ ID NO: 1300 | Polypeptide encoded by SEQ ID NO: 1299 | 30 aa |
| SEQ ID NO: 1301 | MAGE-3 segment 11 | 90 nts |
| SEQ ID NO: 1302 | Polypeptide encoded by SEQ ID NO: 1301 | 30 aa |
| SEQ ID NO: 1303 | MAGE-3 segment 12 | 90 nts |
| SEQ ID NO: 1304 | Polypeptide encoded by SEQ ID NO: 1303 | 30 aa |
| SEQ ID NO: 1305 | MAGE-3 segment 13 | 90 nts |
| SEQ ID NO: 1306 | Polypeptide encoded by SEQ ID NO: 1305 | 30 aa |
| SEQ ID NO: 1307 | MAGE-3 segment 14 | 90 nts |
| SEQ ID NO: 1308 | Polypeptide encoded by SEQ ID NO: 1307 | 30 aa |
| SEQ ID NO: 1309 | MAGE-3 segment 15 | 90 nts |
| SEQ ID NO: 1310 | Polypeptide encoded by SEQ ID NO: 1309 | 30 aa |
| SEQ ID NO: 1311 | MAGE-3 segment 16 | 90 nts |
| SEQ ID NO: 1312 | Polypeptide encoded by SEQ ID NO: 1311 | 30 aa |
| SEQ ID NO: 1313 | MAGE-3 segment 17 | 90 nts |
| SEQ ID NO: 1314 | Polypeptide encoded by SEQ ID NO: 1313 | 30 aa |
| SEQ ID NO: 1315 | MAGE-3 segment 18 | 90 nts |
| SEQ ID NO: 1316 | Polypeptide encoded by SEQ ID NO: 1315 | 30 aa |
| SEQ ID NO: 1317 | MAGE-3 segment 19 | 90 nts |
| SEQ ID NO: 1318 | Polypeptide encoded by SEQ ID NO: 1317 | 30 aa |

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| SEQUENCE ID NUMBER | SEQUENCE | LIMOTH |
|-----------------------|--|--------|
| SEQ ID NO: 1319 | MAGE-3 segment 20 | 90 nts |
| SEQ ID NO: 1320 | Polypeptide encoded by SEQ ID NO: 1319 | 30 aa |
| SEQ ID NO: 1321 | MAGE-3 segment 21 | 54 nts |
| SEQ ID NO: 1322 | Polypeptide encoded by SEQ ID NO: 1321 | 18 aa |
| SEQ ID NO: 1323 | PRAME segment 1 | 90 nts |
| SEQ ID NO: 1324 | Polypeptide encoded by SEQ ID NO: 1323 | 30 aa |
| SEQ ID NO: 1325 | PRAME segment 2 | 90 nts |
| SEQ ID NO: 1326 | Polypeptide encoded by SEQ ID NO: 1325 | 30 aa |
| SEQ ID NO: 1327 | PRAME segment 3 | 90 nts |
| SEQ ID NO: 1328 | Polypeptide encoded by SEQ ID NO: 1327 | 30 aa |
| SEQ ID NO: 1329 | PRAME segment 4 - | 90 nts |
| SEQ ID NO: 1330 | Polypeptide encoded by SEQ ID NO: 1329 | 30 aa |
| SEQ ID NO: 1331 | PRAME segment 5 | 90 nts |
| SEQ ID NO: 1332 | Polypeptide encoded by SEQ ID NO: 1331 | 30 aa |
| SEQ ID NO: 1333 | PRAME segment 6 | 90 nts |
| SEQ ID NO: 1334 | Polypeptide encoded by SEQ ID NO: 1333 | 30 aa |
| SEQ ID NO: 1335 | PRAME segment 7 | 90 nts |
| SEQ ID NO: 1336 | Polypeptide encoded by SEQ ID NO: 1335 | 30 aa |
| SEQ ID NO: 1337 | PRAME segment 8 | 90 nts |
| SEQ ID NO: 1338 | Polypeptide encoded by SEQ ID NO: 1337 | 30 aa |
| SEQ ID NO: 1339 | PRAME segment 9 | 90 nts |
| SEQ ID NO: 1340 | Polypeptide encoded by SEQ ID NO: 1339 | 30 aa |
| SEQ ID NO: 1341 | PRAME segment 10 | 90 nts |
| SEQ ID NO: 1342 | Polypeptide encoded by SEQ ID NO: 1341 | 30 aa |

| SEQUENCE ID NUMBER | SIQUINCI | LENGTH |
|-----------------------|--|--------------------|
| SEQ ID NO: 1343 | PRAME segment 11 | 90 nts |
| SEQ ID NO: 1344 | Polypeptide encoded by SEQ ID NO: 1343 | 30 aa |
| SEQ ID NO: 1345 | PRAME segment 12 | 90 nts |
| SEQ ID NO: 1346 | Polypeptide encoded by SEQ ID NO: 1345 | 30 aa |
| SEQ ID NO: 1347 | PRAME segment 13 | 90 nts |
| SEQ ID NO: 1348 | Polypeptide encoded by SEQ ID NO: 1347 | 30 aa |
| SEQ ID NO: 1349 | PRAME segment 14 | 90 nts |
| SEQ ID NO: 1350 | Polypeptide encoded by SEQ ID NO: 1349 | 30 aa |
| SEQ ID NO: 1351 | PRAME segment 15 | 90 nts |
| SEQ ID NO: 1352 | Polypeptide encoded by SEQ ID NO: 1351 | 30 aa |
| SEQ ID NO: 1353 | PRAME segment 16. | 90 nts |
| SEQ ID NO: 1354 | Polypeptide encoded by SEQ ID NO: 1353 | 30 ⁻ aa |
| SEQ ID NO: 1355 | PRAME segment 17 | 90 nts |
| SEQ ID NO: 1356 | Polypeptide encoded by SEQ ID NO: 1355 | 30 aa |
| SEQ ID NO: 1357 | PRAME segment 18 | 90 nts |
| SEQ ID NO: 1358 | Polypeptide encoded by SEQ ID NO: 1357 | 30 aa |
| SEQ ID NO: 1359 | PRAME segment 19 | 90 nts |
| SEQ ID NO: 1360 | Polypeptide encoded by SEQ ID NO: 1359 | 30 aa |
| SEQ ID NO: 1361 | PRAME segment 20 | 90 nts |
| SEQ ID NO: 1362 | Polypeptide encoded by SEQ ID NO: 1361 | 30 aa |
| SEQ ID NO: 1363 | PRAME segment 21 | 90 nts |
| SEQ ID NO: 1364 | Polypeptide encoded by SEQ ID NO: 1363 | 30 aa |
| SEQ ID NO: 1365 | PRAME segment 22 | 90 nts |
| SEQ ID NO: 1366 | Polypeptide encoded by SEQ ID NO: 1365 | 30 aa |

| MQUENCI ID NUMBER | SEQUENCE | LENGTH |
|----------------------|--|--------|
| SEQ ID NO: 1367 | PRAME segment 23 | 90 nts |
| SEQ ID NO: 1368 | Polypeptide encoded by SEQ ID NO: 1367 | 30 aa |
| SEQ ID NO: 1369 | PRAME segment 24 | 90 nts |
| SEQ ID NO: 1370 | Polypeptide encoded by SEQ ID NO: 1369 | 30 aa |
| SEQ ID NO: 1371 | PRAME segment 25 | 90 nts |
| SEQ ID NO: 1372 | Polypeptide encoded by SEQ ID NO: 1371 | 30 aa |
| SEQ ID NO: 1373 | PRAME segment 26 | 90 nts |
| SEQ ID NO: 1374 | Polypeptide encoded by SEQ ID NO: 1373 | 30 aa |
| SEQ ID NO: 1375 | PRAME segment 27 | 90 nts |
| SEQ ID NO: 1376 | Polypeptide encoded by SEQ ID NO: 1375 | 30 aa |
| SEQ ID NO: 1377 | PRAME segment 28 | 90 nts |
| SEQ ID NO: 1378 | Polypeptide encoded by SEQ ID NO: 1377 | 30 aa |
| SEQ ID NO: 1379 | PRAME segment 29 | 90 nts |
| SEQ ID NO: 1380 | Polypeptide encoded by SEQ ID NO: 1379 | 30 aa |
| SEQ ID NO: 1381 | PRAME segment 30 | 90 nts |
| SEQ ID NO: 1382 | Polypeptide encoded by SEQ ID NO: 1381 | 30 aa |
| SEQ ID NO: 1383 | PRAME segment 31 | 90 nts |
| SEQ ID NO: 1384 | Polypeptide encoded by SEQ ID NO: 1383 | 30 aa |
| SEQ ID NO: 1385 | PRAME segment 32 | 90 nts |
| SEQ ID NO: 1386 | Polypeptide encoded by SEQ ID NO: 1385 | 30 aa |
| SEQ ID NO: 1387 | PRAME segment 33 | 90 nts |
| SEQ ID NO: 1388 | Polypeptide encoded by SEQ ID NO: 1387 | 30 aa |
| SEQ ID NO: 1389 | PRAME segment 34 | 54 nts |
| SEQ ID NO: 1390 | Polypeptide encoded by SEQ ID NO: 1389 | 18 aa |

| SEQUENCE ID NUMBER | SEQUENCE | LENGTH |
|-----------------------|--|--------|
| SEQ ID NO: 1391 | TRP2IN2 segment 1 | 90 nts |
| SEQ ID NO: 1392 | Polypeptide encoded by SEQ ID NO: 1391 | 30 aa |
| SEQ ID NO: 1393 | TRP2IN2 segment 2 | 90 nts |
| SEQ ID NO: 1394 | Polypeptide encoded by SEQ ID NO: 1393 | 30 aa |
| SEQ ID NO: 1395 | TRP2IN2 segment 3 | 84 nts |
| SEQ ID NO: 1396 | Polypeptide encoded by SEQ ID NO: 1395 | 28 aa |
| SEQ ID NO: 1397 | NYNSO1a segment 1 | 90 nts |
| SEQ ID NO: 1398 | Polypeptide encoded by SEQ ID NO: 1397 | 30 aa |
| SEQ ID NO: 1399 | NYNSO1a segment 2 | 90 nts |
| SEQ ID NO: 1400 | Polypeptide encoded by SEQ ID NO: 1399 | 30 aa |
| SEQ ID NO: 1401 | NYNSO1a segment 3 | 90 nts |
| SEQ ID NO: 1402 | Polypeptide encoded by SEQ ID NO: 1401 | 30 aa |
| SEQ ID NO: 1403 | NYNSO1a segment 4 90 nts | |
| SEQ ID NO: 1404 | Polypeptide encoded by SEQ ID NO: 1403 30 aa | |
| SEQ ID NO: 1405 | NYNSO1a segment 5 90 nts | |
| SEQ ID NO: 1406 | Polypeptide encoded by SEQ ID NO: 1405 | 30 aa |
| SEQ ID NO: 1407 | NYNSO1a segment 6 | 90 nts |
| SEQ ID NO: 1408 | Polypeptide encoded by SEQ ID NO: 1407 | 30 aa |
| SEQ ID NO: 1409 | NYNSO1a segment 7 | 90 nts |
| SEQ ID NO: 1410 | Polypeptide encoded by SEQ ID NO: 1409 | 30 aa |
| SEQ ID NO: 1411 | NYNSO1a segment 8 90 nts | |
| SEQ ID NO: 1412 | Polypeptide encoded by SEQ ID NO: 1411 30 aa | |
| SEQ ID NO: 1413 | NYNSO1a segment 9 | 90 nts |
| SEQ ID NO: 1414 | Polypeptide encoded by SEQ ID NO: 1413 | 30 aa |

| SEQUENCE ID NUMBER | SEQUENCE | LENGTH |
|-----------------------|--|--------|
| SEQ ID NO: 1415 | NYNSO1a segment 10 | 90 nts |
| SEQ ID NO: 1416 | Polypeptide encoded by SEQ ID NO: 1415 | 30 aa |
| SEQ ID NO: 1417 | NYNSO1a segment 11 | 90 nts |
| SEQ ID NO: 1418 | Polypeptide encoded by SEQ ID NO: 1417 | 30 aa |
| SEQ ID NO: 1419 | NYNSO1a segment 12 | 57 nts |
| SEQ ID NO: 1420 | Polypeptide encoded by SEQ ID NO: 1419 | 19 aa |
| SEQ ID NO: 1421 | NYNSO1b segment 1 | 90 nts |
| SEQ ID NO: 1422 | Polypeptide encoded by SEQ ID NO: 1421 | 30 aa |
| SEQ ID NO: 1423 | NYNSO1b segment 2 | 90 nts |
| SEQ ID NO: 1424 | Polypeptide encoded by SEQ ID NO: 1423 | 30 aa |
| SEQ ID NO: 1425 | NYNSO1b segment 3 | 90 nts |
| SEQ ID NO: 1426 | Polypeptide encoded by SEQ ID NO: 1425 | 30 aa |
| SEQ ID NO: 1427 | NYNSO1b segment 4 | 51 nts |
| SEQ ID NO: 1428 | Polypeptide encoded by SEQ ID NO: 1427 | |
| SEQ ID NO: 1429 | LAGE1 segment 1 | 90 nts |
| SEQ ID NO: 1430 | Polypeptide encoded by SEQ ID NO: 1429 | 30 aa |
| SEQ ID NO: 1431 | LAGE1 segment 2 | 90 nts |
| SEQ ID NO: 1432 | Polypeptide encoded by SEQ ID NO: 1431 | 30 aa |
| SEQ ID NO: 1433 | LAGE1 segment 3 | 90 nts |
| SEQ ID NO: 1434 | Polypeptide encoded by SEQ ID NO: 1433 | 30 aa |
| SEQ ID NO: 1435 | LAGE1 segment 4 | 90 nts |
| SEQ ID NO: 1436 | Polypeptide encoded by SEQ ID NO: 1435 | 30 aa |
| SEQ ID NO: 1437 | LAGE1 segment 5 | 90 nts |
| SEQ ID NO: 1438 | Polypeptide encoded by SEQ ID NO: 1437 | 30 aa |

| SEQUENCE ID NUMBER | STQUE CI | LEMGTH |
|-----------------------|--|-----------|
| SEQ ID NO: 1439 | LAGE1 segment 6 | 90 nts |
| SEQ ID NO: 1440 | Polypeptide encoded by SEQ ID NO: 1439 | 30 aa |
| SEQ ID NO: 1441 | LAGE1 segment 7 | 90 nts |
| SEQ ID NO: 1442 | Polypeptide encoded by SEQ ID NO: 1441 | 30 aa |
| SEQ ID NO: 1443 | LAGE1 segment 8 | 90 nts |
| SEQ ID NO: 1444 | Polypeptide encoded by SEQ ID NO: 1443 | 30 aa |
| SEQ ID NO: 1445 | LAGE1 segment 9 | 90 nts |
| SEQ ID NO: 1446 | Polypeptide encoded by SEQ ID NO: 1445 | 30 aa |
| SEQ ID NO: 1447 | LAGE1 segment 10 | 90 nts |
| SEQ ID NO: 1448 | Polypeptide encoded by SEQ ID NO: 1447 | 30 aa |
| SEQ ID NO: 1449 | LAGE1 segment 11 | 90 nts |
| SEQ ID NO: 1450 | Polypeptide encoded by SEQ ID NO: 1449 30 aa | |
| SEQ ID NO: 1451 | LAGE1 segment 12 | 57 nts |
| SEQ ID NO: 1452 | Polypeptide encoded by SEQ ID NO: 1451 19 aa | |
| SEQ ID NO: 1453 | Melanoma cancer specific Savine | 10623 nts |
| SEQ ID NO: 1454 | Polypeptide encoded by SEQ ID NO: 1453 | 3541 aa |
| SEQ ID NO: 1455 | Figure 16 A1S1 99mer | 99 nts |
| SEQ ID NO: 1456 | Figure 16 A1S2 100mer | 100 nts |
| SEQ ID NO: 1457 | Figure 16 A1S3 100mer | 100 nts |
| SEQ ID NO: 1458 | Figure 16 A1S4 100mer | 100 nts |
| SEQ ID NO: 1459 | Figure 16 A1S5 100mer | 100 nts |
| SEQ ID NO: 1460 | Figure 16 A1S6 99mer | 99 nts |
| SEQ ID NO: 1461 | Figure 16 A1S7 97mer | 99 nts |
| SEQ ID NO: 1462 | Figure 16 A1S8 100mer | 100 nts |

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| SEQUENCE ID NUMBER | SEQUENCE LING | |
|-----------------------|--|---------|
| SEQ ID NO: 1463 | Figure 16 A1S9 100mer | 100 nts |
| SEQ ID NO: 1464 | Figure 16 A1S10 75mer | 76 nts |
| SEQ ID NO: 1465 | Figure 16 A1F 20mer | 20 nts |
| SEQ ID NO: 1466 | Figure 16 A1R 20mer | 20 nts |
| SEQ ID NO: 1467 | Amino acid sequence of immunostimulatory domain of an invasin protein from Yersinia spp. | 16 aa |

DETAILED DESCRIPTION OF THE INVENTION

1. Definitions

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The articles "a" and "an" are used herein to refer to one or to more than one (i.e., to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

As used herein, the term "about" refers to a quantity, level, value, dimension, size, or amount that varies by as much as 30%, preferably by as much as 20%, and more preferably by as much as 10% to a reference quantity, level, value, dimension, size, or amount.

By "antigen-binding molecule" is meant a molecule that has binding affinity for a target antigen. It will be understood that this term extends to immunoglobulins, immunoglobulin fragments and non-immunoglobulin derived protein frameworks that exhibit antigen-binding activity.

The term "clade" as used herein refers to a hypothetical species of an organism and its descendants or a monophyletic group of organisms. Clades carry a definition, based on ancestry, and a diagnosis, based on synapomorphies. It should be noted that diagnoses of clades could change while definitions do not.

Throughout this specification, unless the context requires otherwise, the words "comprise", "comprises" and "comprising" will be understood to imply the inclusion of a stated step or element or group of steps or elements but not the exclusion of any other step or element or group of steps or elements.

By "expression vector" is meant any autonomous genetic element capable of directing the synthesis of a protein encoded by the vector. Such expression vectors are known by practitioners in the art.

As used herein, the term "function" refers to a biological, enzymatic, or therapeutic function.

"Homology" refers to the percentage number of amino acids that are identical or constitute conservative substitutions as defined in Table B infra. Homology may be determined using sequence comparison programs such as GAP (Deveraux et al. 1984, Nucleic Acids Research 12, 387-395). In this way, sequences of a similar or substantially different length to those cited herein might be compared by insertion of gaps into the alignment, such gaps being determined, for example, by the comparison algorithm used by GAP.

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To enhance an immune response ("immunoenhancement"), as is well-known in the art, means to increase an animal's capacity to respond to foreign or disease-specific antigens (e.g., cancer antigens) i.e., those cells primed to attack such antigens are increased in number, activity, and ability to detect and destroy the those antigens. Strength of immune response is measured by standard tests including: direct measurement of peripheral blood lymphocytes by means known to the art; natural killer cell cytotoxicity assays (see, e.g., Provinciali M. et al (1992, J. Immunol. Meth. 155: 19-24), cell proliferation assays (see, e.g., Vollenweider, I. and Groseurth, P. J. (1992, J. Immunol. Meth. 149: 133-135), immunoassays of immune cells and subsets (see, e.g., Loeffler, D. A., et al. (1992, Cytom. 13: 169-174); Rivoltini, L., et al. (1992, Can. Immunol. Immunother. 34: 241-251); or skin tests for cell-mediated immunity (see, e.g., Chang, A. E. et al (1993, Cancer Res. 53: 1043-1050). Any statistically significant increase in strength of immune response as measured by the foregoing tests is considered "enhanced immune response" "immunoenhancement" or "immunopotentiation" as used herein. Enhanced immune response is also indicated by physical manifestations such as fever and inflammation, as well as healing of systemic and local infections, and reduction of symptoms in disease, i.e., decrease in tumour size, alleviation of symptoms of a disease or condition including, but not restricted to, leprosy, tuberculosis, malaria, naphthous ulcers, herpetic and papillomatous warts, gingivitis, artherosclerosis, the concomitants of AIDS such as Kaposi's sarcoma, bronchial infections, and the like. Such physical manifestations also define "enhanced immune response" "immunoenhancement" or "immunopotentiation" as used herein.

30 Reference herein to "immuno-interactive" includes reference to any interaction, reaction, or other form of association between molecules and in particular where one of the molecules is, or mimics, a component of the immune system.

By "isolated" is meant material that is substantially or essentially free from components that normally accompany it in its native state.

By "modulating" is meant increasing or decreasing, either directly or indirectly, an immune response against a target antigen of a member selected from the group consisting of a cancer and an organism, preferably a pathogenic organism.

By "natural gene" is meant a gene that naturally encodes a protein.

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The term "natural polypeptide" as used herein refers to a polypeptide that exists in nature.

By "obtained from" is meant that a sample such as, for example, a polynucleotide
extract or polypeptide extract is isolated from, or derived from, a particular source of the
host. For example, the extract can be obtained from a tissue or a biological fluid isolated
directly from the host.

The term "oligonucleotide" as used herein refers to a polymer composed of a multiplicity of nucleotide residues (deoxyribonucleotides or ribonucleotides, or related structural variants or synthetic analogues thereof) linked via phosphodiester bonds (or related structural variants or synthetic analogues thereof). Thus, while the term "oligonucleotide" typically refers to a nucleotide polymer in which the nucleotide residues and linkages between them are naturally occurring, it will be understood that the term also includes within its scope various analogues including, but not restricted to, peptide nucleic acids (PNAs), phosphoramidates, phosphorothioates, methyl phosphonates, 2-O-methyl ribonucleic acids, and the like. The exact size of the molecule can vary depending on the particular application. An oligonucleotide is typically rather short in length, generally from about 10 to 30 nucleotide residues, but the term can refer to molecules of any length, although the term "polynucleotide" or "nucleic acid" is typically used for large oligonucleotides.

By "operably linked" is meant that transcriptional and translational regulatory polynucleotides are positioned relative to a polypeptide-encoding polynucleotide in such a manner that the polynucleotide is transcribed and the polypeptide is translated.

The term "parent polypeptide" as used herein typically refers to a polypeptide encoded by a natural gene. However, it is possible that the parent polypeptide corresponds to a protein that is not naturally-occurring but has been engineered using recombinant techniques. In this instance, a polynucleotide encoding the parent polypeptide may comprise different but synonymous codons relative to a natural gene encoding the same polypeptide. Alternatively, the parent polypeptide may not correspond to a natural polypeptide sequence. For example, the parent polypeptide may comprise one or more consensus sequences common to a plurality of polypeptides.

The term "patient" refers to patients of human or other mammal and includes any individual it is desired to examine or treat using the methods of the invention. However, it will be understood that "patient" does not imply that symptoms are present. Suitable mammals that fall within the scope of the invention include, but are not restricted to, primates, livestock animals (e.g., sheep, cows, horses, donkeys, pigs), laboratory test animals (e.g., rabbits, mice, rats, guinea pigs, hamsters), companion animals (e.g., cats, dogs) and captive wild animals (e.g., foxes, deer, dingoes).

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By "pharmaceutically-acceptable carrier" is meant a solid or liquid filler, diluent or encapsulating substance that can be safely used in topical or systemic administration to a mammal.

"Polypeptide", "peptide" and "protein" are used interchangeably herein to refer to a polymer of amino acid residues and to variants and synthetic analogues of the same. Thus, these terms apply to amino acid polymers in which one or more amino acid residues is a synthetic non-naturally occurring amino acid, such as a chemical analogue of a corresponding naturally occurring amino acid, as well as to naturally-occurring amino acid polymers.

The term "polynucleotide" or "nucleic acid" as used herein designates mRNA, RNA, cRNA, cDNA or DNA. The term typically refers to oligonucleotides greater than 30 nucleotide residues in length.

By "primer" is meant an oligonucleotide which, when paired with a strand of DNA, is capable of initiating the synthesis of a primer extension product in the presence of a suitable polymerising agent. The primer is preferably single-stranded for maximum

efficiency in amplification but can alternatively be double-stranded. A primer must be sufficiently long to prime the synthesis of extension products in the presence of the polymerisation agent. The length of the primer depends on many factors, including application, temperature to be employed, template reaction conditions, other reagents, and source of primers. For example, depending on the complexity of the target sequence, the oligonucleotide primer typically contains 15 to 35 or more nucleotide residues, although it can contain fewer nucleotide residues. Primers can be large polynucleotides, such as from about 35 nucleotides to several kilobases or more. Primers can be selected to be "substantially complementary" to the sequence on the template to which it is designed to hybridise and serve as a site for the initiation of synthesis. By "substantially complementary", it is meant that the primer is sufficiently complementary to hybridise with a target polynucleotide. Preferably, the primer contains no mismatches with the template to which it is designed to hybridise but this is not essential. For example, noncomplementary nucleotide residues can be attached to the 5' end of the primer, with the remainder of the primer sequence being complementary to the template. Alternatively, non-complementary nucleotide residues or a stretch of non-complementary nucleotide residues can be interspersed into a primer, provided that the primer sequence has sufficient complementarity with the sequence of the template to hybridise therewith and thereby form a template for synthesis of the extension product of the primer.

"Probe" refers to a molecule that binds to a specific sequence or sub-sequence or other moiety of another molecule. Unless otherwise indicated, the term "probe" typically refers to a polynucleotide probe that binds to another polynucleotide, often called the "target polynucleotide", through complementary base pairing. Probes can bind target polynucleotides lacking complete sequence complementarity with the probe, depending on the stringency of the hybridisation conditions. Probes can be labelled directly or indirectly.

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By "recombinant polypeptide" is meant a polypeptide made using recombinant techniques, i.e., through the expression of a recombinant or synthetic polynucleotide.

Terms used to describe sequence relationships between two or more polynucleotides or polypeptides include "reference sequence", "comparison window", "sequence identity", "percentage of sequence identity" and "substantial identity". A "reference sequence" is at least 12 but frequently 15 to 18 and often at least 25 monomer

units, inclusive of nucleotides and amino acid residues, in length. Because two polynucleotides may each comprise (1) a sequence (i.e., only a portion of the complete polynucleotide sequence) that is similar between the two polynucleotides, and (2) a sequence that is divergent between the two polynucleotides, sequence comparisons between two (or more) polynucleotides are typically performed by comparing sequences of the two polynucleotides over a "comparison window" to identify and compare local regions of sequence similarity. A "comparison window" refers to a conceptual segment of at least 50 contiguous positions, usually about 50 to about 100, more usually about 100 to about 150 in which a sequence is compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. The comparison window may comprise additions or deletions (i.e., gaps) of about 20% or less as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. Optimal alignment of sequences for aligning a comparison window may be conducted by computerised implementations of algorithms (GAP, 15 BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Drive Madison, WI, USA) or by inspection and the best alignment (i.e., resulting in the highest percentage homology over the comparison window) generated by any of the various methods selected. Reference also may be made to the BLAST family of programs as for example disclosed by Altschul et al., 1997, Nucl. Acids Res. 25:3389. A detailed discussion of sequence analysis can be found in Unit 19.3 of Ausubel et al., "Current Protocols in Molecular Biology", John Wiley & Sons Inc, 1994-1998, Chapter 15.

The term "sequence identity" as used herein refers to the extent that sequences are identical on a nucleotide-by-nucleotide basis or an amino acid-by-amino acid basis over a window of comparison. Thus, a "percentage of sequence identity" is calculated by comparing two optimally aligned sequences over the window of comparison, determining the number of positions at which the identical nucleic acid base (e.g., A, T, C, G, I) or the identical amino acid residue (e.g., Ala, Pro, Ser, Thr, Gly, Val, Leu, Ile, Phe, Tyr, Trp, Lys, Arg, His, Asp, Glu, Asn, Gln, Cys and Met) occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison (i.e., the window size), and multiplying the result by 100 to yield the percentage of sequence identity. For the purposes of the present

invention, "sequence identity" will be understood to mean the "match percentage" calculated by the DNASIS computer program (Version 2.5 for windows; available from Hitachi Software engineering Co., Ltd., South San Francisco, California, USA) using standard defaults as used in the reference manual accompanying the software.

The term "synthetic polynucleotide" as used herein refers to a polynucleotide formed in vitro by the manipulation of a polynucleotide into a form not normally found in nature. For example, the synthetic polynucleotide can be in the form of an expression vector. Generally, such expression vectors include transcriptional and translational regulatory polynucleotide operably linked to the polynucleotide.

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The term "synonymous codon" as used herein refers to a codon having a different nucleotide sequence than another codon but encoding the same amino acid as that other codon.

By "translational efficiency" is meant the efficiency of a cell's protein synthesis machinery to incorporate the amino acid encoded by a codon into a nascent polypeptide chain. This efficiency can be evidenced, for example, by the rate at which the cell is able to synthesise the polypeptide from an RNA template comprising the codon, or by the amount of the polypeptide synthesised from such a template.

By "vector" is meant a polynucleotide molecule, preferably a DNA molecule derived, for example, from a plasmid, bacteriophage, yeast or virus, into which a polynucleotide can be inserted or cloned. A vector preferably contains one or more unique restriction sites and can be capable of autonomous replication in a defined host cell including a target cell or tissue or a progenitor cell or tissue thereof, or be integrable with the genome of the defined host such that the cloned sequence is reproducible. Accordingly, the vector can be an autonomously replicating vector, i.e., a vector that exists as an extrachromosomal entity, the replication of which is independent of chromosomal replication, e.g., a linear or closed circular plasmid, an extrachromosomal element, a minichromosome, or an artificial chromosome. The vector can contain any means for assuring self-replication. Alternatively, the vector can be one which, when introduced into the host cell, is integrated into the genome and replicated together with the chromosome(s) into which it has been integrated. A vector system can comprise a single vector or plasmid, two or more vectors or plasmids, which together contain the total DNA to be introduced

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into the genome of the host cell, or a transposon. The choice of the vector will typically depend on the compatibility of the vector with the host cell into which the vector is to be introduced. In the present case, the vector is preferably a viral or viral-derived vector, which is operably functional in animal and preferably mammalian cells. Such vector may be derived from a poxvirus, an adenovirus or yeast. The vector can also include a selection marker such as an antibiotic resistance gene that can be used for selection of suitable transformants. Examples of such resistance genes are known to those of skill in the art and include the *nptII* gene that confers resistance to the antibiotics kanamycin and G418 (Geneticin®) and the *hph* gene which confers resistance to the antibiotic hygromycin B.

2. Synthetic polypeptides

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The inventors have surprisingly discovered that the structure of a parent polypeptide can be disrupted sufficiently to impede, abrogate or otherwise alter at least one function of the parent polypeptide, while simultaneously minimising the destruction of potentially useful epitopes that are present in the parent polypeptide, by fusing, coupling or otherwise linking together different segments of the parent polypeptide in a different relationship relative to their linkage in the parent polypeptide. As a result of this change in relationship, the sequence of the linked segments in the resulting synthetic polypeptide is different to a sequence contained within the parent polypeptide. The synthetic polypeptides of the invention are useful as immunopotentiating agents, and are referred to elsewhere in the specification as scrambled antigen vaccines, super attenuated vaccines or "Savines".

Thus, the invention broadly resides in a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein said segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

It is preferable but not essential that the segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to that of corresponding segments in said at least one parent polypeptide. For example, in the case of a parent polypeptide that comprises three contiguous or overlapping segments A-B-C-D, these segments may be linked in 23 other possible orders to form a synthetic polypeptide. These orders may be selected from the group consisting of: A-B-D-C, A-C-B-D, A-C-D-B, A-D-B-C, A-D-C-B, B-A-C-D, B-A-D-C, B-C-A-D, B-C-D-A, B-D-A-C, B-D-C-A, C-A-B-D, C-A-D-B, C-B-A-D, C-B-D-A, C-D-B-A, D-A-B-C, D-A-C-B, D-B-A-C, D-B-C-A, D-C-A-B, and D-C-B-A. Although the rearrangement of the segments is preferably random, it is especially preferable to exclude or otherwise minimise rearrangements that result in complete or partial reassembly of the parent sequence (e.g., ADBC, BACD, DABC). It will be appreciated, however, that the probability of such complete or partial reassembly diminishes as the number of segments for rearrangement increases.

The order of the segments is suitably shuffled, reordered or otherwise rearranged relative to the order in which they exist in the parent polypeptide so that the structure of the polypeptide is disrupted sufficiently to impede, abrogate or otherwise alter at least one

function associated with the parent polypeptide. Preferably, the segments of the parent polypeptide are randomly rearranged in the synthetic polypeptide.

The parent polypeptide is suitably a polypeptide that is associated with a disease or condition. For example, the parent polypeptide may be a polypeptide expressed by a pathogenic organism or a cancer. Alternatively, the parent polypeptide can be a self peptide related to an autoimmune disease including, but are not limited to, diseases such as diabetes (e.g., juvenile diabetes), multiple sclerosis, rheumatoid arthritis, myasthenia gravis, atopic dermatitis, and psoriasis and ankylosing spondylitis. Accordingly, the synthetic molecules of the present invention may also have utility for the induction of tolerance in a subject afflicted with an autoimmune disease or condition or with an allergy or other condition to which tolerance is desired. For example tolerance may be induced by contacting an immature dendritic cell of the individual to be treated with a synthetic polypeptide of the invention or by expressing in an immature dendritic cell a synthetic polynucleotide of the invention. Tolerance may also be induced against antigens causing allergic responses (e.g., asthma, hay fever). In this case, the parent polypeptide is suitably an allergenic protein including, but not restricted to, house-dust-mite allergenic proteins as for example described by Thomas and Smith (1998, Allergy, 53(9): 821-832).

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The pathogenic organism includes, but is not restricted to, yeast, a virus, a bacterium, and a parasite. Any natural host of the pathogenic organism is contemplated by the present invention and includes, but is not limited to, mammals, avians and fish. In a preferred embodiment, the pathogenic organism is a virus, which may be an RNA virus or a DNA virus. Preferably, the RNA virus is Human Immunodeficiency Virus (HIV), Poliovirus, and Influenza virus, Rous sarcoma virus, or a Flavivirus such as Japanese encephalitis virus. In a preferred embodiment, the RNA virus is a Hepatitis virus including, but not limited to, Hepatitis strains A, B and C. Suitably, the DNA virus is a Herpesvirus including, but not limited to, Herpes simplex virus, Epstein-Barr virus, Cytomegalovirus and Parvovirus. In a preferred embodiment, the virus is HIV and the parent polypeptide is suitably selected from env, gag, pol, vif, vpr, tat, rev, vpu and nef, or combination thereof. In an alternate preferred embodiment, the virus is Hepatitis C1a virus and the parent polypeptide is the Hepatitis C1a virus polyprotein.

In another embodiment, the pathogenic organism is a bacterium, which includes, but is not restricted to, *Neisseria* species, *Meningococcal* species, *Haemophilus* species *Salmonella* species, *Streptococcal* species, *Legionella* species and *Mycobacterium* species.

In yet another embodiment, the pathogenic organism is a parasite, which includes, but is not restricted to, *Plasmodium* species, *Schistosoma* species, *Leishmania* species, *Trypanosoma* species, *Toxoplasma* species and *Giardia* species.

Any cancer or tumour is contemplated by the present invention. For example, the cancer or tumour includes, but is not restricted to, melanoma, lung cancer, breast cancer, cervical cancer, prostate cancer, colon cancer, pancreatic cancer, stomach cancer, bladder cancer, kidney cancer, post transplant lymphoproliferative disease (PTLD), Hodgkin's Lymphoma and the like. Preferably, the cancer or tumour relates to melanoma. In a preferred embodiment of this type, the parent polypeptide is a melanocyte differentiation antigen which is suitably selected from gp100, MART, TRP-1, Tyros, TRP2, MC1R, MUC1F, MUC1R or a combination thereof. In an alternate preferred embodiment of this type, the parent polypeptide is a melanoma-specific antigen which is suitably selected from BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b, LAGE1 or a combination thereof.

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In a preferred embodiment, the segments are selected on the basis of size. A segment according to the invention may be of any suitable size that can be utilised to elicit an immune response against an antigen encoded by the parent polypeptide. A number of factors can influence the choice of segment size. For example, the size of a segment should be preferably chosen such that it includes, or corresponds to the size of, T cell epitopes and their processing requirement. Practitioners in the art will recognise that class I-restricted T cell epitopes can be between 8 and 10 amino acids in length and if placed next to unnatural flanking residues, such epitopes can generally require 2 to 3 natural flanking amino acids to ensure that they are efficiently processed and presented. Class II-restricted T cell epitopes can range between 12 and 25 amino acids in length and may not require natural flanking residues for efficient proteolytic processing although it is believed that natural flanking residues may play a role. Another important feature of class II-restricted epitopes is that they generally contain a core of 9-10 amino acids in the middle which bind specifically to class II MHC molecules with flanking sequences either side of this core

stabilising binding by associating with conserved structures on either side of class II MHC antigens in a sequence independent manner (Brown et al., 1993). Thus the functional region of class II-restricted epitopes is typically less than 15 amino acids long. The size of linear B cell epitopes and the factors effecting their processing, like class II-restricted epitopes, are quite variable although such epitopes are frequently smaller in size than 15 amino acids. From the foregoing, it is preferable, but not essential, that the size of the segment is at least 4 amino acids, preferably at least 7 amino acids, more preferably at least 12 amino acids, more preferably at least 20 amino acids and more preferably at least 30 amino acids. Suitably, the size of the segment is less than 2000 amino acids, more preferably less than 1000 amino acids, more preferably less than 500 amino acids, more preferably less than 200 amino acids, more preferably less than 100 amino acids, more preferably less than 80 amino acids and even more preferably less than 60 amino acids and still even more preferably less than 40 amino acids. In this regard, it is preferable that the size of the segments is as small as possible so that the synthetic polypeptide adopts a 15 functionally different structure relative to the structure of the parent polypeptide. It is also preferable that the size of the segments is large enough to minimise loss of T cell epitopes. In an especially preferred embodiment, the size of the segment is about 30 amino acids.

An optional spacer may be utilised to space adjacent segments relative to each other. Accordingly, an optional spacer may be interposed between some or all of the segments. The spacer suitably alters proteolytic processing and/or presentation of adjacent segment(s). In a preferred embodiment of this type, the spacer promotes or otherwise enhances proteolytic processing and/or presentation of adjacent segment(s). Preferably, the spacer comprises at least one amino acid. The at least one amino acid is suitably a neutral amino acid. The neutral amino acid is preferably alanine. Alternatively, the at least one amino acid is cysteine.

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In a preferred embodiment, segments are selected such that they have partial sequence identity or homology with one or more other segments. Suitably, at one or both ends of a respective segment there is comprised at least 4 contiguous amino acids, preferably at least 7 contiguous amino acids, more preferably at least 10 contiguous amino acids, more preferably at least 15 contiguous amino acids and even more preferably at least 20 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments. Preferably, at the or each

end of a respective segment there is comprised less than 500 contiguous amino acids, more preferably less than 200 contiguous amino acids, more preferably less than 100 contiguous amino acids, more preferably less than 50 contiguous amino acids, more preferably less than 40 contiguous amino acids, and even more preferably less than 30 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments. Such sequence overlap (also referred to elsewhere in the specification as "overlapping fragments" or "overlapping segments") is preferable to ensure potential epitopes at segment boundaries are not lost and to ensure that epitopes at or near segment boundaries are processed efficiently if placed beside or near amino acids that inhibit processing. Preferably, the segment size is about twice the size of the overlap.

In a preferred embodiment, when segments have partial sequence homology therebetween, the homologous sequences suitably comprise conserved and/or non-conserved amino acid differences. Exemplary conservative substitutions are listed in the following table.

15 TABLE B

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| Original Residue | Exemples p Substitutions |
|------------------|--------------------------|
| Ala | Ser |
| Arg | Lys |
| Asn | Gln, His |
| Asp | Glu |
| Cys | Ser |
| Gln | Asn |
| Glu | Asp |
| Gly | Pro |
| His | Asn, Gln |
| Ile · | Leu, Val |
| Leu | Ile, Val |

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| Original Residue | Exemplies Substitutions |
|------------------|-------------------------|
| Lys | Arg, Gln, Glu |
| Met | Leu, Ile, |
| Phe | Met, Leu, Tyr |
| Ser | Thr |
| Thr | Ser |
| Trp | Tyr |
| Tyr | Trp, Phe |
| Val . | Ile, Leu |

Conserved or non-conserved differences may correspond to polymorphisms in corresponding parent polypeptides. Polymorphic polypeptides are expressed by various pathogenic organisms and cancers. For example, the polymorphic polypeptides may be expressed by different viral strains or clades or by cancers in different individuals.

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Sequence overlap between respective segments is preferable to minimise destruction of any epitope sequences that may result from any shuffling or rearrangement of the segments relative to their existing order in the parent polypeptide. If overlapping segments as described above are employed to form a synthetic polypeptide, it may not be necessary to change the order in which those segments are linked together relative to the order in which corresponding segments are normally present in the parent polypeptide. In this regard, such overlapping segments when linked together in the synthetic polypeptide can adopt a different structure relative to the structure of the parent polypeptide, wherein the different structure does not provide for one or more functions associated with the parent polypeptide. For example, in the case of four segments A-B-C-D each spanning 30 contiguous amino acids of the parent polypeptide and having a 10-amino acid overlapping sequence with one or more adjacent segments, the synthetic polypeptide will have duplicated 10-amino acid sequences bridging segments A-B, B-C and C-D. The presence of these duplicated sequences may be sufficient to render a different structure and to abrogate or alter function relative to the parent polypeptide.

In a preferred embodiment, segment size is about 30 amino acids and sequence overlap at one or both ends of a respective segment is about 15 amino acids. However, it will be understood that other suitable segment sizes and sequence overlap sizes are contemplated by the present invention, which can be readily ascertained by persons of skill in the art.

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It is preferable but not necessary to utilise all the segments of the parent polypeptide in the construction of the synthetic polypeptide. Suitably, at least 30%, preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, even more preferably at least 80% and still even more preferably at least 90% of the parent polypeptide sequence is used in the construction of the synthetic polypeptide. However, it will be understood that the more sequence information from a parent polypeptide that is utilised to construct the synthetic polypeptide, the greater the population coverage will be of the synthetic polypeptide as an immunogen. Preferably, no sequence information from the parent polypeptide is excluded (e.g., because of an apparent lack of immunological epitopes).

Persons of skill in the art will appreciate that when preparing a synthetic polypeptide against a pathogenic organism (e.g., a virus) or a cancer, it may be preferable to use sequence information from a plurality of different polypeptides expressed by the organism or the cancer. Accordingly, in a preferred embodiment, segments from a plurality of different polypeptides are linked together to form a synthetic polypeptide according to the invention. It is preferable in this respect to utilise as many parent polypeptides as possible from, or in relation to, a particular source in the construction of the synthetic polypeptide. The source of parent polypeptides includes, but is not limited to, a pathogenic organism and a cancer. Suitably, at least about 30%, preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, even more preferably at least 70%, even more preferably at least 80% and still even more preferably at least 90% of the parent polypeptides expressed by the source is used in the construction of the synthetic polypeptide. Preferably, parent polypeptides from a virus include, but are not restricted to, latent polypeptides, regulatory polypeptides or polypeptides expressed early during their replication cycle. Suitably, parent polypeptides from a parasite or bacterium include, but are not restricted to, secretory polypeptides and polypeptides expressed on the surface of

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the parasite or bacteria. It is preferred that parent polypeptides from a cancer or tumour are cancer specific polypeptides.

Suitably, hypervariable sequences within the parent polypeptide are excluded from the construction of the synthetic polypeptide.

The synthetic polypeptides of the inventions may be prepared by any suitable procedure known to those of skill in the art. For example, the polypeptide may be synthesised using solution synthesis or solid phase synthesis as described, for example, in Chapter 9 of Atherton and Shephard (1989, Solid Phase Peptide Synthesis: A Practical Approach. IRL Press, Oxford) and in Roberge et al (1995, Science 269: 202). Syntheses may employ, for example, either t-butyloxycarbonyl 9-(t-Boc) or fluorenylmethyloxycarbonyl (Fmoc) chemistries (see Chapter 9.1, of Coligan et al., CURRENT PROTOCOLS IN PROTEIN SCIENCE, John Wiley & Sons, Inc. 1995-1997; Stewart and Young, 1984, Solid Phase Peptide Synthesis, 2nd ed. Pierce Chemical Co., Rockford, Ill; and Atherton and Shephard, supra).

Alternatively, the polypeptides may be prepared by a procedure including the steps of:

- (a) preparing a synthetic construct including a synthetic polynucleotide encoding a synthetic polypeptide wherein said synthetic polynucleotide is operably linked to a regulatory polynucleotide, wherein said synthetic polypeptide comprises a plurality of different segments of a parent polypeptide, wherein said segments are linked together in a different relationship relative to their linkage in the parent polypeptide;
 - (b) introducing the synthetic construct into a suitable host cell;
- (c) culturing the host cell to express the synthetic polypeptide from said synthetic construct; and
- (d) isolating the synthetic polypeptide.

The synthetic construct is preferably in the form of an expression vector. For example, the expression vector can be a self-replicating extra-chromosomal vector such as a plasmid, or a vector that integrates into a host genome. Typically, the regulatory polynucleotide may include, but is not limited to, promoter sequences, leader or signal

sequences, ribosomal binding sites, transcriptional start and stop sequences, translational start and termination sequences, and enhancer or activator sequences. Constitutive or inducible promoters as known in the art are contemplated by the invention. The promoters may be either naturally occurring promoters, or hybrid promoters that combine elements of more than one promoter. The regulatory polynucleotide will generally be appropriate for the host cell used for expression. Numerous types of appropriate expression vectors and suitable regulatory polynucleotides are known in the art for a variety of host cells.

In a preferred embodiment, the expression vector contains a selectable marker gene to allow the selection of transformed host cells. Selection genes are well known in the art and will vary with the host cell used.

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The expression vector may also include a fusion partner (typically provided by the expression vector) so that the synthetic polypeptide of the invention is expressed as a fusion polypeptide with said fusion partner. The main advantage of fusion partners is that they assist identification and/or purification of said fusion polypeptide. In order to express said fusion polypeptide, it is necessary to ligate a polynucleotide according to the invention into the expression vector so that the translational reading frames of the fusion partner and the polynucleotide coincide.

Well known examples of fusion partners include, but are not limited to, glutathione-S-transferase (GST), Fc portion of human IgG, maltose binding protein (MBP) and hexahistidine (HIS6), which are particularly useful for isolation of the fusion polypeptide by affinity chromatography. For the purposes of fusion polypeptide purification by affinity chromatography, relevant matrices for affinity chromatography are glutathione-, amylose-, and nickel- or cobalt-conjugated resins respectively. Many such matrices are available in "kit" form, such as the QIAexpressTM system (Qiagen) useful with (HIS6) fusion partners and the Pharmacia GST purification system. In a preferred embodiment, the recombinant polynucleotide is expressed in the commercial vector pFLAGTM.

Another fusion partner well known in the art is green fluorescent protein (GFP). This fusion partner serves as a fluorescent "tag" which allows the fusion polypeptide of the invention to be identified by fluorescence microscopy or by flow cytometry. The GFP tag is useful when assessing subcellular localisation of a fusion polypeptide of the invention,

or for isolating cells which express a fusion polypeptide of the invention. Flow cytometric methods such as fluorescence activated cell sorting (FACS) are particularly useful in this latter application. Preferably, the fusion partners also have protease cleavage sites, such as for Factor X₂, Thrombin and inteins (protein introns), which allow the relevant protease to partially digest the fusion polypeptide of the invention and thereby liberate the recombinant polypeptide of the invention therefrom. The liberated polypeptide can then be isolated from the fusion partner by subsequent chromatographic separation. Fusion partners according to the invention also include within their scope "epitope tags", which are usually short peptide sequences for which a specific antibody is available. Well known examples of epitope tags for which specific monoclonal antibodies are readily available include c-Myc, influenza virus, haemagglutinin and FLAG tags. Alternatively, a fusion partner may be provided to promote other forms of immunity. For example, the fusion partner may be an antigen-binding molecule that is immuno-interactive with a conformational epitope on a target antigen or to a post-translational modification of a target antigen (e.g., an antigen-binding molecule that is immuno-interactive with a glycosylated target antigen).

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The step of introducing the synthetic construct into the host cell may be effected by any suitable method including transfection, and transformation, the choice of which will be dependent on the host cell employed. Such methods are well known to those of skill in the art.

Synthetic polypeptides of the invention may be produced by culturing a host cell transformed with the synthetic construct. The conditions appropriate for protein expression will vary with the choice of expression vector and the host cell. This is easily ascertained by one skilled in the art through routine experimentation.

Suitable host cells for expression may be prokaryotic or eukaryotic. One preferred host cell for expression of a polypeptide according to the invention is a bacterium. The bacterium used may be *Escherichia coli*. Alternatively, the host cell may be an insect cell such as, for example, *SF9* cells that may be utilised with a baculovirus expression system.

The synthetic polypeptide may be conveniently prepared by a person skilled in the art using standard protocols as for example described in Sambrook, *et al.*, MOLECULAR CLONING. A LABORATORY MANUAL (Cold Spring Harbor Press, 1989), in particular

Sections 16 and 17; Ausubel et al., CURRENT PROTOCOLS IN MOLECULAR BIOLOGY (John Wiley & Sons, Inc. 1994-1998), in particular Chapters 10 and 16; and Coligan et al., CURRENT PROTOCOLS IN PROTEIN SCIENCE (John Wiley & Sons, Inc. 1995-1997), in particular Chapters 1, 5 and 6.

The amino acids of the synthetic polypeptide can be any non-naturally occurring or any naturally occurring amino acid. Examples of unnatural amino acids and derivatives during peptide synthesis include but are not limited to, use of 4-amino butyric acid, 6-aminohexanoic acid, 4-amino-3-hydroxy-5-phenylpentanoic acid, 4-amino-3-hydroxy-6-methylheptanoic acid, t-butylglycine, norleucine, norvaline, phenylglycine, ornithine, sarcosine, 2-thienyl alanine and/or D-isomers of amino acids. A list of unnatural amino acids contemplated by the present invention is shown in TABLE C.

TABLE C

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| . Mon=conventional amine asid | Men-conventional animo setd |
|-------------------------------|-----------------------------|
| α-aminobutyric acid | L-N-methylalanine |
| α-amino-α-methylbutyrate | L-N-methylarginine |
| aminocyclopropane-carboxylate | L-N-methylasparagine |
| aminoisobutyric acid | L-N-methylaspartic acid |
| aminonorbornyl-carboxylate | L-N-methylcysteine |
| cyclohexylalanine | L-N-methylglutamine |
| cyclopentylalanine | L-N-methylglutamic acid |
| L-N-methylisoleucine | L-N-methylhistidine |
| D-alanine | L-N-methylleucine |
| D-arginine | L-N-methyllysine |
| D-aspartic acid | L-N-methylmethionine |
| D-cysteine | L-N-methylnorleucine |
| D-glutamate | L-N-methylnorvaline |
| D-glutamic acid | L-N-methylomithine |

| Non-convendenal amine sold | Non-conventional animo acti |
|----------------------------|-----------------------------|
| D-histidine | L-N-methylphenylalanine |
| D-isoleucine | L-N-methylproline |
| D-leucine | L-N-medlylserine |
| D-lysine | L-N-methylthreonine |
| D-methionine | L-N-methyltryptophan |
| D-ornithine | L-N-methyltyrosine |
| D-phenylalanine | L-N-methylvaline |
| D-proline | L-N-methylethylglycine |
| D-serine | L-N-methyl-t-butylglycine |
| D-threonine | L-norleucine |
| D-tryptophan | L-norvaline |
| D-tyrosine | α-methyl-aminoisobutyrate |
| D-valine | α-methyl-γ-aminobutyrate |
| D-α-methylalanine | α-methylcyclohexylalanine |
| D-α-methylarginine | α-methylcylcopentylalanine |
| D-α-methylasparagine | α-methyl-α-napthylalanine |
| D-α-methylaspartate | α-methylpenicillamine |
| D-α-methylcysteine | N-(4-aminobutyl)glycine |
| D-α-methylglutamine | N-(2-aminoethyl)glycine |
| D-α-methylhistidine | N-(3-aminopropyl)glycine |
| D-α-methylisoleucine | N-amino-α-methylbutyrate |
| D-α-methylleucine | α-napthylalanine |
| D-α-methyllysine | N-benzylglycine |
| D-α-methylmethionine | N-(2-carbamylediyl)glycine |
| D-α-methylomithiine | N-(carbamylmethyl)glycine |

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| Non-conventional ammo edd | Nen-conveniend emine acid |
|--|---|
| D-α-methylphenylalanine | N-(2-carboxyethyl)glycine |
| D-α-methylproline | N-(carboxymethyl)glycine |
| D-α-methylserine | N-cyclobutylglycine |
| D-α-methylthreonine | N-cycloheptylglycine |
| D-o-methyltryptophan | N-cyclohexylglycine |
| D-α-methyltyrosine | N-cyclodecylglycine |
| L-a-methylleucine | L-\a-methyllysine |
| L-α-methylmethionine | L-a-methylnorleucine |
| L-α-methylnorvatine | L-a-methylomithine |
| L-α-methylphenylalanine | L-α-methylproline |
| L-\a-methylserine | L-α-methylthreonine |
| L-α-methyltryptophan | L-α-methyltyrosine |
| L-a-methylvaline | L-N-methylhomophenylalanine |
| N-(N-(2,2-diphenylethyl carbamylmethyl)glycine | N-(N-(3,3-diphenylpropyl carbamylmethyl)glycine |
| 1-carboxy-1-(2,2-diphenyl-ethyl amino)cyclopropane | |

The invention also contemplates modifying the synthetic polypeptides of the invention using ordinary molecular biological techniques so as to alter their resistance to proteolytic degradation or to optimise solubility properties or to render them more suitable as an immunogenic agent.

3. Preparation of synthetic polynucleotides of the invention

The invention contemplates synthetic polynucleotides encoding the synthetic polypeptides as for example described in Section 2 supra. Polynucleotides encoding segments of a parent polypeptide can be produced by any suitable technique. For example, such polynucleotides can be synthesised de novo using readily available machinery.

Sequential synthesis of DNA is described, for example, in U.S. Patent No 4,293,652. Instead of de novo synthesis, recombinant techniques may be employed including use of restriction endonucleases to cleave a polynucleotide encoding at least a segment of the parent polypeptide and use of ligases to ligate together in frame a plurality of cleaved polynucleotides encoding different segments of the parent polypeptide. Suitable recombinant techniques are described for example in the relevant sections of Ausubel, et al. (supra) and of Sambrook, et al., (supra) which are incorporated herein by reference. Preferably, the synthetic polynucleotide is constructed using splicing by overlapping extension (SOEing) as for example described by Horton et al. (1990, Biotechniques 8(5): 528-535; 1995, Mol Biotechnol. 3(2): 93-99; and 1997, Methods Mol Biol. 67: 141-149). However, it should be noted that the present invention is not dependent on, and not directed to, any one particular technique for constructing the synthetic construct.

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Various modifications to the synthetic polynucleotides may be introduced as a means of increasing intracellular stability and half-life. Possible modifications include but are not limited to the addition of flanking sequences of ribo- or deoxy- nucleotides to the 5' and/or 3' ends of the molecule or the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages within the oligodeoxyribonucleotide backbone.

The invention therefore contemplates a method of producing a synthetic polynucleotide as broadly described above, comprising linking together in the same reading frame at least two nucleic acid sequences encoding different segments of a parent polypeptide to form a synthetic polynucleotide, which encodes a synthetic polypeptide according to the invention. Suitably, nucleic acid sequences encoding at least 10 segments, preferably at least 20 segments, more preferably at least 40 segments and more preferably at least 100 segments of a parent polypeptide are employed to produce the synthetic polynucleotide.

Preferably, the method further comprises selecting segments of the parent polypeptide, reverse translating the selected segments and preparing nucleic acid sequences encoding the selected segments. It is preferred that the method further comprises randomly linking the nucleic acid sequences together to form the synthetic polynucleotide. The nucleic acid sequences may be oligonucleotides or polynucleotides.

Suitably, segments are selected on the basis of size. Additionally, or in the alternative, segments are selected such that they have partial sequence identity or homology (i.e., sequence overlap) with one or more other segments. A number of factors can influence segment size and sequence overlap as mentioned above. In the case of sequence overlap, large amounts of duplicated nucleic acid sequences can sometimes result in sections of nucleic acid being lost during nucleic acid amplification (e.g., polymerase chain reaction, PCR) of such sequences, recombinant plasmid propagation in a bacterial host or during amplification of recombinant viruses containing such sequences. Accordingly, in a preferred embodiment, nucleic acid sequences encoding segments having sequence identity or homology with one or more other encoded segments are not linked together in an arrangement in which the identical or homologous sequences are contiguous. Also, it is preferable that different codons are used to encode a specific amino acid in a duplicated region. In this context, an amino acid of a parent polypeptide sequence is preferably reverse translated to provide a codon which, in the context of adjacent or local 15 sequence elements, has a lower propensity of forming an undesirable sequence (e.g., a duplicated sequence or a palindromic sequence) that is refractory to the execution of a task (e.g., cloning or sequencing). Alternatively, segments may be selected such that they contain a carboxyl terminal leucine residue or such that reverse translated sequences encoding the segments contain restriction enzyme sites for convenient splicing of the reverse translated sequences.

The method optionally further comprises linking a spacer oligonucleotide encoding at least one spacer residue between segment-encoding nucleic acids. Such spacer residue(s) may be advantageous in ensuring that epitopes within the segments are processed and presented efficiently. Preferably, the spacer oligonucleotide encodes 2 to 3 spacer residues. The spacer residue is suitably a neutral amino acid, which is preferably alanine.

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Optionally, the method further comprises linking in the same reading frame as other segment-containing nucleic acid sequences at least one variant nucleic acid sequence which encodes a variant segment having a homologous but not identical amino acid sequence relative to other encoded segments. Suitably, the variant segment comprises conserved and/or non-conserved amino acid differences relative to one or more other encoded segments. Such differences may correspond to polymorphisms as discussed above. In a preferred embodiment, degenerate bases are designed or built in to the at least one variant nucleic acid sequence to give rise to all desired homologous sequences.

When a large number of polymorphisms is intended to be covered, it is preferred that multiple synthetic polynucleotides are constructed rather than a single synthetic polynucleotide, which encodes all variant segments. For example, if there is less than 85% homology between polymorphic polypeptides, then it is preferred that more than one synthetic polynucleotide is constructed.

Preferably, the method further comprises optimising the codon composition of the synthetic polynucleotide such that it is translated efficiently by a host cell. In this regard, it is well known that the translational efficiency of different codons varies between organisms and that such differences in codon usage can be utilised to enhance the level of protein expression in a particular organism. In this regard, reference may be made to Seed et al. (International Application Publication No WO 96/09378) who disclose the replacement of existing codons in a parent polynucleotide with synonymous codons to enhance expression of viral polypeptides in mammalian host cells. Preferably, the first or second most frequently used codons are employed for codon optimisation.

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Preferably, gene splicing by overlap extension or "gene SOEing" (supra) is employed for the construction of the synthetic polynucleotide which is a PCR-based method of recombining DNA sequences without reliance on restriction sites and of directly generating mutated DNA fragments in vitro. By modifying the sequences incorporated into the 5'-ends of the primers, any pair of PCR products can be made to share a common sequence at one end. Under PCR conditions, the common sequence allows strands from two different fragments to hybridise to one another, forming an overlap. Extension of this overlap by DNA polymerase yields a recombinant molecule. However, a problem with long synthetic constructs is that mutations generally incorporate into amplified products during synthesis. In this instance, it is preferred that resolvase treatment is employed at various steps of the synthesis. Resolvases are bacteriophage-encoded endonucleases which recognise disruptions or mispairing of double stranded DNA and are primarily used by bacteriophages to resolve Holliday junctions (Mizuuchi, 1982; Youil et al., 1995). For example, T7 endonuclease I can be employed in synthetic DNA constructions to recognise mutations and cleave corrupted dsDNA. The mutated DNA strands are then hybridised to

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non-mutant or correct DNA sequences, which results in a mispairing of DNA bases. The mispaired bases are recognised by the resolvase, which then cleaves the DNA nearby leaving only correctly hybridised sequences intact. Preferably a thermostable resolvase enzyme is employed during splicing or amplification so that errors are not incorporated in downstream synthesis products.

Synthetic polynucleotides according to the invention can be operably linked to a regulatory polynucleotide in the form a synthetic construct as for example described in Section 2 supra. Synthetic constructs of the invention have utility inter alia as nucleic acid vaccines. The choice of regulatory polynucleotide and synthetic construct will depend on the intended host.

Exemplary expression vectors for expression of a synthetic polypeptide according to the invention include, but are not restricted to, modified Ankara Vaccinia virus as for example described by Allen et al. (2000, J. Immunol. 164(9): 4968-4978), fowlpox virus as for example described by Boyle and Coupar (1988, Virus Res. 10: 343-356) and the herpes simplex amplicons described for example by Fong et al. in U.S. Patent No. 6,051,428. Alternatively, Adenovirus and Epstein-Barr virus vectors, which are preferably capable of accepting large amounts of DNA or RNA sequence information, can be used.

Preferred promoter sequences that can be utilised for expression of synthetic polypeptides include the P7.5 or PE/L promoters as for example disclosed by Kumar and 20 Boyle. (1990, Virology 179: 151-158), CMV and RSV promoters.

The synthetic construct optionally further includes a nucleic acid sequence encoding an immunostimulatory molecule. The immunostimulatory molecule may be fusion partner of the synthetic polypeptide. Alternatively, the immunostimulatory molecule may be translated separately from the synthetic polypeptide. Preferably, the immunostimulatory molecule comprises a general immunostimulatory peptide sequence. For example, the immunostimulatory peptide sequence may comprise a domain of an invasin protein (Inv) from the bacteria *Yersinia* spp as for example disclosed by Brett *et al.* (1993, *Eur. J. Immunol.* 23: 1608-1614). This immune stimulatory property results from the capability of this invasin domain to interact with the β1 integrin molecules present on T cells, particularly activated immune or memory T cells. A preferred embodiment of the invasin domain (Inv) for linkage to a synthetic polypeptide has been previously described

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in U.S. Pat. No. 5,759,551. The said Inv domain has the sequence: Thr-Ala-Lys-Ser-Lys-Lys-Phe-Pro-Ser-Tyr-Thr-Ala-Thr-Tyr-Gln-Phe [SEQ ID NO; 1467] or is an immune stimulatory homologue thereof from the corresponding region in another Yersinia species invasin protein. Such homologues thus may contain substitutions, deletions or insertions of amino acid residues to accommodate strain to strain variation, provided that the homologues retain immune stimulatory properties. The general immunostimulatory sequence may optionally be linked to the synthetic polypeptide by a spacer sequence.

In an alternate embodiment, the immunostimulatory molecule may comprise an immunostimulatory membrane or soluble molecule, which is suitably a T cell costimulatory molecule. Preferably, the T cell co-stimulatory molecule is a B7 molecule or a biologically active fragment thereof, or a variant or derivative of these. The B7 molecule includes, but is not restricted to, B7-1 and B7-2. Preferably, the B7 molecule is B7-1. Alternatively, the T cell co-stimulatory molecule may be an ICAM molecule such as ICAM-1 and ICAM-2.

In another embodiment, the immunostimulatory molecule can be a cytokine. which includes, but is not restricted to, an interleukin, a lymphokine, tumour necrosis factor and an interferon. Alternatively, the immunostimulatory molecule may comprise an immunomodulatory oligonucleotide as for example disclosed by Krieg in U.S. Patent No. 6,008,200.

Suitably, the size of the synthetic polynucleotide does not exceed the ability of host cells to transcribe, translate or proteolytically process and present epitopes to the immune system. Practitioners in the art will also recognise that the size of the synthetic polynucleotide can impact on the capacity of an expression vector to express the synthetic polynucleotide in a host cell. In this connection, it is known that the efficacy of DNA 25 vaccination reduces with expression vectors greater that 20-kb. In such situations it is preferred that a larger number of smaller synthetic constructs is utilised rather than a single large synthetic construct.

4. Immunopotentiating compositions

invention also contemplates a composition, comprising immunopotentiating agent selected from the group consisting of a synthetic polypeptide as 30

described in Section 2, and a synthetic polynucleotide or a synthetic construct as described in Section 3, together with a pharmaceutically acceptable carrier. One or more immunopotentiating agents can be used as actives in the preparation of immunopotentiating compositions. Such preparation uses routine methods known to persons skilled in the art. Typically, such compositions are prepared as injectables, either as liquid solutions or suspensions; solid forms suitable for solution in, or suspension in, liquid prior to injection may also be prepared. The preparation may also be emulsified. The active immunogenic ingredients are often mixed with excipients that are pharmaceutically acceptable and compatible with the active ingredient. Suitable excipients are, for example, water, saline, dextrose, glycerol, ethanol, or the like and combinations thereof. In addition, if desired, the vaccine may contain minor amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents, and/or adjuvants that enhance the effectiveness of the vaccine. Examples of adjuvants which may be effective include but are not limited to: aluminium hydroxide, N-acetyl-muramyl-L-threonyl-D-isoglutamine (thur-MDP), Nacetyl-nor-muramyl-L-alanyl-D-isoglutamine (CGP 11637, referred to as nor-MDP), Nacetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3hydroxyphosphoryloxy)-ethylamine (CGP 1983A, referred to as MTP-PE), and RIBI, which contains three components extracted from bacteria, monophosphoryl lipid A, trehalose dimycolate and cell wall skeleton (MPL+TDM+CWS) in a 2% squalene/Tween 80 emulsion. For example, the effectiveness of an adjuvant may be determined by measuring the amount of antibodies resulting from the administration of the composition, wherein those antibodies are directed against one or more antigens presented by the treated cells of the composition.

The immunopotentiating agents may be formulated into a composition as neutral or salt forms. Pharmaceutically acceptable salts include the acid addition salts (formed with free amino groups of the peptide) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids such as acetic, oxalic, tartaric, maleic, and the like. Salts formed with the free carboxyl groups may also be derived from inorganic basis such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic basis as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine, and the like.

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If desired, devices or compositions containing the immunopotentiating agents suitable for sustained or intermittent release could be, in effect, implanted in the body or topically applied thereto for the relatively slow release of such materials into the body.

The compositions are conventionally administered parenterally, by injection, for example, either subcutaneously or intramuscularly. Additional formulations which are suitable for other modes of administration include suppositories and, in some cases, oral formulations. For suppositories, traditional binders and carriers may include, for example, polyalkylene glycols or triglycerides; such suppositories may be formed from mixtures containing the active ingredient in the range of 0.5% to 10%, preferably 1%-2%. Oral formulations include such normally employed excipients as, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium carbonate, and the like. These compositions take the form of solutions, suspensions, tablets, pills, capsules, sustained release formulations or powders and contain 10%-95% of active ingredient, preferably 25%-70%.

Administration of the gene therapy construct to said mammal, preferably a human, may include delivery via direct oral intake, systemic injection, or delivery to selected tissue(s) or cells, or indirectly via delivery to cells isolated from the mammal or a compatible donor. An example of the latter approach would be stem cell therapy, wherein isolated stem cells having potential for growth and differentiation are transfected with the vector comprising the *Sox18* nucleic acid. The stem cells are cultured for a period and then transferred to the mammal being treated.

With regard to nucleic acid based compositions, all modes of delivery of such compositions are contemplated by the present invention. Delivery of these compositions to cells or tissues of an animal may be facilitated by microprojectile bombardment, liposome mediated transfection (e.g., lipofectin or lipofectamine), electroporation, calcium phosphate or DEAE-dextran-mediated transfection, for example. In an alternate embodiment, a synthetic construct may be used as a therapeutic or prophylactic composition in the form of a "naked DNA" composition as is known in the art. A discussion of suitable delivery methods may be found in Chapter 9 of CURRENT PROTOCOLS IN MOLECULAR BIOLOGY (Eds. Ausubel et al.; John Wiley & Sons Inc., 1997 Edition) or on the Internet site DNAvaccine.com. The compositions may be administered by intradermal (e.g., using panjetTM delivery) or intramuscular routes.

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The step of introducing the synthetic polynucleotide into a target cell will differ depending on the intended use and species, and can involve one or more of non-viral and viral vectors, cationic liposomes, retroviruses, and adenoviruses such as, for example, described in Mulligan, R.C., (1993 Science 260 926-932) which is hereby incorporated by reference. Such methods can include, for example:

- A. Local application of the synthetic polynucleotide by injection (Wolff et al., 1990, Science 247 1465-1468, which is hereby incorporated by reference), surgical implantation, instillation or any other means. This method can also be used in combination with local application by injection, surgical implantation, instillation or any other means, of cells responsive to the protein encoded by the synthetic polynucleotide so as to increase the effectiveness of that treatment. This method can also be used in combination with local application by injection, surgical implantation, instillation or any other means, of another factor or factors required for the activity of said protein.
- B. General systemic delivery by injection of DNA, (Calabretta et al., 1993, Cancer Treat. Rev. 19 169-179, which is incorporated herein by reference), or RNA, alone or in combination with liposomes (Zhu et al., 1993, Science 261 209-212, which is incorporated herein by reference), viral capsids or nanoparticles (Bertling et al., 1991, Biotech. Appl. Biochem. 13 390-405, which is incorporated herein by reference) or any other mediator of delivery. Improved targeting might be achieved by linking the synthetic polynucleotide to a targeting molecule (the so-called "magic bullet" approach employing, for example, an antibody), or by local application by injection, surgical implantation or any other means, of another factor or factors required for the activity of the protein encoding said synthetic polynucleotide, or of cells responsive to said protein.
 - C. Injection or implantation or delivery by any means, of cells that have been modified ex vivo by transfection (for example, in the presence of calcium phosphate: Chen et al., 1987, Mole. Cell Biochem. 7 2745-2752, or of cationic lipids and polyamines: Rose et al., 1991, BioTech. 10 520-525, which articles are incorporated herein by reference), infection, injection, electroporation (Shigekawa et al., 1988, BioTech. 6 742-751, which is incorporated herein by reference) or any other way so as to increase the

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expression of said synthetic polynucleotide in those cells. The modification can be mediated by plasmid, bacteriophage, cosmid, viral (such as adenoviral or retroviral; Mulligan, 1993, Science 260 926-932; Miller, 1992, Nature 357 455-460; Salmons et al., 1993, Hum. Gen. Ther. 4 129-141, which articles are incorporated herein by reference) or other vectors, or other agents of modification such as liposomes (Zhu et al., 1993, Science 261 209-212, which is incorporated herein by reference), viral capsids or nanoparticles (Bertling et al., 1991, Biotech. Appl. Biochem. 13 390-405, which is incorporated herein by reference), or any other mediator of modification. The use of cells as a delivery vehicle for genes or gene products has been described by Barr et al., 1991, Science 254 1507-1512 and by Dhawan et al., 1991, Science 254 1509-1512, which articles are incorporated herein by reference. Treated cells can be delivered in combination with any nutrient, growth factor, matrix or other agent that will promote their survival in the treated subject.

Also encapsulated by the present invention is a method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment a therapeutically effective amount of a composition as broadly described above. The disease or condition may be caused by a pathogenic organism or a cancer as for example described above.

In a preferred embodiment, the immunopotentiating composition of the invention is suitable for treatment of, or prophylaxis against, a cancer. Cancers which could be suitably treated in accordance with the practices of this invention include cancers of the lung, breast, ovary, cervix, colon, head and neck, pancreas, prostate, stomach, bladder, kidney, bone liver, oesophagus, brain, testicle, uterus, melanoma and the various leukemias and lymphomas.

In an alternate embodiment, the immunopotentiating composition is suitable for treatment of, or prophylaxis against, a viral, bacterial or parasitic infection. Viral infections contemplated by the present invention include, but are not restricted to, infections caused by HIV, Hepatitis, Influenza, Japanese encephalitis virus, Epstein-Barr virus and respiratory syncytial virus. Bacterial infections include, but are not restricted to, those caused by Neisseria species, Meningococcal species, Haemophilus species Salmonella species, Streptococcal species, Legionella species and Mycobacterium species. Parasitic

infections encompassed by the invention include, but are not restricted to, those caused by *Plasmodium* species, *Schistosoma* species, *Leishmania* species, *Trypanosoma* species, *Toxoplasma* species and *Giardia* species.

The above compositions or vaccines may be administered in a manner compatible

with the dosage formulation, and in such amount as is therapeutically effective to alleviate
patients from the disease or condition or as is prophylactically effective to prevent
incidence of the disease or condition in the patient. The dose administered to a patient, in
the context of the present invention, should be sufficient to effect a beneficial response in a
patient over time such as a reduction or cessation of blood loss. The quantity of the
composition or vaccine to be administered may depend on the subject to be treated
inclusive of the age, sex, weight and general health condition thereof. In this regard,
precise amounts of the composition or vaccine for administration will depend on the
judgement of the practitioner. In determining the effective amount of the composition or
vaccine to be administered in the treatment of a disease or condition, the physician may
evaluate the progression of the disease or condition over time. In any event, those of skill
in the art may readily determine suitable dosages of the composition or vaccine of the
invention.

In a preferred embodiment, DNA-based immunopotentiating agent (e.g., 100 μ g) is delivered intradermally into a patient at day 1 and at week 8 to prime the patient. A recombinant poxvirus (e.g., at 10^7 pfu/mL) from which substantially the same immunopotentiating agent can be expressed is then delivered intradermally as a booster at weeks 16 and 24, respectively.

The effectiveness of the immunisation may be assessed using any suitable technique. For example, CTL lysis assays may be employed using stimulated splenocytes or peripheral blood mononuclear cells (PBMC) on peptide coated or recombinant virus infected cells using ⁵¹Cr labelled target cells. Such assays can be performed using for example primate, mouse or human cells (Allen et al., 2000, J. Immunol. 164(9): 4968-4978 also Woodberry et al., infra). Alternatively, the efficacy of the immunisation may be monitored using one or more techniques including, but not limited to, HLA class I Tetramer staining - of both fresh and stimulated PBMCs (see for example Allen et al., supra), proliferation assays (Allen et al., supra), ElispotTM Assays and intracellular INF-

gamma staining (Allen et al., supra), ELISA Assays - for linear B cell responses; and Western blots of cell sample expressing the synthetic polynucleotides.

5. Computer related embodiments

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The design or construction of a synthetic polypeptide sequence or a synthetic polynucleotide sequence according to the invention is suitably facilitated with the assistance of a computer programmed with software, which inter alia fragments a parent sequence into fragments, and which links those fragments together in a different relationship relative to their linkage in the parent sequence. The ready use of a parent sequence for the construction of a desired synthetic molecule according to the invention requires that it be stored in a computer-readable format. Thus, in accordance with the present invention, sequence data relating to a parent molecule (e.g., a parent polypeptide) is stored in a machine-readable storage medium, which is capable of processing the data to fragment the sequence of the parent molecule into fragments and to link together the fragments in a different relationship relative to their linkage in the parent molecule.

Therefore, another embodiment of the present invention provides a machinereadable data storage medium, comprising a data storage material encoded with machine readable data which, when used by a machine programmed with instructions for using said data, fragments a parent sequence into fragments, and links those fragments together in a different relationship relative to their linkage in the parent sequence. In a preferred 20 embodiment of this type, a machine-readable data storage medium is provided that is capable of reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding the fragment and to link together in the same reading frame each of the nucleic acid sequences to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in a parent polypeptide sequence.

In another embodiment, the invention encompasses a computer for designing the sequence of a synthetic polypeptide and/or a synthetic polynucleotide of the invention, wherein the computer comprises wherein said computer comprises: (a) a machine readable data storage medium comprising a data storage material encoded with machine readable data, wherein said machine readable data comprises the sequence of a parent polypeptide; (b) a working memory for storing instructions for processing said machine-readable data;

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(c) a central-processing unit coupled to said working memory and to said machine-readable data storage medium, for processing said machine-readable data into said synthetic polypeptide sequence and/or said synthetic polynucleotide; and (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence and/or said synthetic polynucleotide.

In yet another embodiment, the invention contemplates a computer program product for designing the sequence of a synthetic polynucleotide of the invention, comprising code that receives as input the sequence of a parent polypeptide, code that fragments the sequence of the parent polypeptide into fragments, code that reverse translates the sequence of a respective fragment to provide a nucleic acid sequence encoding the fragment, code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the parent polypeptide sequence, and a computer readable medium that stores the codes.

A version of these embodiments is presented in Figure 23, which shows a system 10 including a computer 11 comprising a central processing unit ("CPU") 20, a working memory 22 which may be, e.g., RAM (random-access memory) or "core" memory, mass storage memory 24 (such as one or more disk drives or CD-ROM drives), one or more cathode-ray tube ("CRT") display terminals 26, one or more keyboards 28, one or more input lines 30, and one or more output lines 40, all of which are interconnected by a conventional bidirectional system bus 50.

Input hardware 36, coupled to computer 11 by input lines 30, may be implemented in a variety of ways. For example, machine-readable data of this invention may be inputted via the use of a modem or modems 32 connected by a telephone line or dedicated data line 34. Alternatively or additionally, the input hardware 36 may comprise CD. Alternatively, ROM drives or disk drives 24 in conjunction with display terminal 26, keyboard 28 may also be used as an input device.

Output hardware 46, coupled to computer 11 by output lines 40, may similarly be implemented by conventional devices. By way of example, output hardware 46 may include CRT display terminal 26 for displaying a synthetic polynucleotide sequence or a synthetic polypeptide sequence as described herein. Output hardware might also include a

printer 42, so that hard copy output may be produced, or a disk drive 24, to store system output for later use.

In operation, CPU 20 coordinates the use of the various input and output devices 36,46 coordinates data accesses from mass storage 24 and accesses to and from working memory 22, and determines the sequence of data processing steps. A number of programs may be used to process the machine readable data of this invention. Exemplary programs may use for example the steps outlined in the flow diagram illustrated in Figure 24. Broadly, these steps include (1) inputting at least one parent polypeptide sequence; (2) optionally adding to alanine spacers at the ends of each polypeptide sequence; (3) fragmenting the polypeptide sequences into fragments (e.g., 30 amino acids long), which are preferably overlapping (e.g., by 15 amino acids); (4) reverse translating the fragment to provide a nucleic acid sequence for each fragment and preferably using for the reverse translation first and second most translationally efficient codons for a cell type, wherein the codons are preferably alternated out of frame with each other in the overlaps of consecutive fragments; (5) randomly rearranging the fragments; (6) checking whether rearranged fragments recreate at least a portion of a parent polypeptide sequence; (7) repeating randomly rearranging the fragments when rearranged fragments recreate said at least a portion; or otherwise (8) linking the rearranged fragments together to produce a synthetic polypeptide sequence and/or a synthetic polynucleotide sequence; and (9) outputting said synthetic polypeptide sequence and/or a synthetic polynucleotide sequence. An example of an algorithm which uses inter alia the aforementioned steps is shown in Figure 25. By way of example, this algorithm has been used for the design of synthetic polynucleotides and synthetic polypeptides according to the present invention for Hepatitis C 1a and for melanoma, as illustrated in Figures 26 and 27.

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Figure 28 shows a cross section of a magnetic data storage medium 100 which can be encoded with machine readable data, or set of instructions, for designing a synthetic molecule of the invention, which can be carried out by a system such as system 10 of Figure 23. Medium 100 can be a conventional floppy diskette or hard disk, having a suitable substrate 101, which may be conventional, and a suitable coating 102, which may be conventional, on one or both sides, containing magnetic domains (not visible) whose polarity or orientation can be altered magnetically. Medium 100 may also have an opening (not shown) for receiving the spindle of a disk drive or other data storage device 24. The

magnetic domains of coating 102 of medium 100 are polarised or oriented so as to encode in manner which may be conventional, machine readable data such as that described herein, for execution by a system such as system 10 of Figure 23.

Figure 29 shows a cross section of an optically readable data storage medium 110 5 which also can be encoded with such a machine-readable data, or set of instructions, for designing a synthetic molecule of the invention, which can be carried out by a system such as system 10 of Figure 23. Medium 110 can be a conventional compact disk read only memory (CD-ROM) or a rewritable medium such as a magneto-optical disk, which is optically readable and magneto-optically writable. Medium 100 preferably has a suitable substrate 111, which may be conventional, and a suitable coating 112, which may be conventional, usually of one side of substrate 111.

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In the case of CD-ROM, as is well known, coating 112 is reflective and is impressed with a plurality of pits 113 to encode the machine-readable data. The arrangement of pits is read by reflecting laser light off the surface of coating 112. A protective coating 114, which preferably is substantially transparent, is provided on top of coating 112.

In the case of a magneto-optical disk, as is well known, coating 112 has no pits 113, but has a plurality of magnetic domains whose polarity or orientation can be changed magnetically when heated above a certain temperature, as by a laser (not shown). The orientation of the domains can be read by measuring the polarisation of laser light reflected from coating 112. The arrangement of the domains encodes the data as described above.

In order that the invention may be readily understood and put into practical effect, particular preferred non-limiting embodiments will now be described as follows.

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EXAMPLES

EXAMPLE 1

Preparation of an HIV Savine

Experimental Protocol

5 Plasmids

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The plasmid pDNAVacc is ampicillin resistant and contains an expression cassette comprising a CMV promoter and enhancer, a synthetic intron, a multiple cloning site (MCS) and a SV40poly A signal sequence (Thomson *et al.*, 1998). The plasmid pTK7.5 and contains a selection cassette, a pox virus 7.5 early/late promoter and a MCS flanked on either side by Vaccinia virus TK gene sequences.

Recombinant Vaccinia Viruses

Recombinant Vaccinia viruses expressing the gag, env (IIB) and pol (LAI) genes of HIV-1 were used as previously described and denoted VV-GAG, VV-POL, VV-ENV (Woodberry et al., 1999; Kent et al., 1998).

15 Marker Rescue Recombination

Recombinant Vaccinia viruses containing Savine constructs were generated by marker rescue recombination, using protocols described previously (Boyle et al., 1985). Plaque purified viruses were tested for the TK phenotype and for the appropriate genome arrangement by Southern blot and PCR.

20 Oligonucleotides

Oligonucleotides 50 nmol scale and desalted were purchased from Life Technologies. Short oligonucleotides were resuspended in 100 µL of water, their concentration determined, then diluted to 20 µM for use in PCR or sequencing reactions. Long oligonucleotides for splicing reactions were denatured for 5 minutes at 94°C in 25 µL of formamide loading buffer then 0.5 µL gel purified on a 6% polyacrylamide gel.

Gel slices containing full-length oligonucleotides were visualised with ethidium bromide, excised, placed in EppendorfTM tubes, combined with 200 μL of water before being crushed using the plunger of a 1 mL syringe. Before being used in splicing reactions the crushed gel was resuspended in an appropriate volume of buffer and 1-2 μL of the resuspendate used directly in the splicing reactions.

Sequencing

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Sequencing was performed using Dye terminator sequencing reactions and analyzed by the Biomedical Resource Facility at the John Curtin School of Medical Research using an ABI automated sequencer.

10 Restimulation of Lymphocytes from HIV Infected Patients

Two pools of recombinant Vaccinia viruses containing VV-AC1 + VV-BC1 (Pool 1) or VV-AC2 + VV-BC2 + VV-CC2 (Pool 2) were used to restimulate lymphocytes from the blood samples of HIV-infected patients. Briefly CTL lines were generated from HIV-infected donor PBMC. A fifth of the total PBMC were infected with either Pool 1 or Pool 2 Vaccinia viruses then added back to the original cell suspension. The infected cell suspension was then cultured with IL-7 for 1 week.

CTL Assays

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Restimulated PBMCs were used as effectors in a standard ⁵¹Cr-release CTL assay.

Targets were autologous EBV-transformed lymphoblastoid cell lines (LCLs) infected with

the following viruses: Pool 1, Pool 2,VV-GAG, VV-POL or VV-ENV. Assay controls included uninfected targets, targets infected with VV-lacZ (virus control) and K562 cells.

Results

HIV Savine Design

A main goal of the Savine strategy is to include as much protein sequence information from a pathogen or cancer as possible in such a way that potential T cell epitopes remain intact and so that the vaccine or therapy is extremely safe. An HIV Savine is described herein not only to compare this strategy to other strategies but also, to produce

an HIV vaccine that would provide the maximum possible population coverage as well as catering for the major HIV clades.

A number of design criteria was first determined to exploit the many advantages of using a synthetic approach. One advantage is that it is possible to use consensus protein sequences to design these vaccines. Using consensus sequences for a highly variable virus like HTV should provide better vaccine coverage because individual viral isolate sequences may have lost epitopes which induce CTL against the majority of other viral isolates. Thus, using the consensus sequences of each HIV clade rather than individual isolate sequences should provide better vaccine coverage. Taking this one step further, a consensus sequence that covers all HIV clades should theoretically provide better coverage than using just the consensus sequences for individual clades. Before designing such a sequence however, it was decided that a more appropriate and focussed HIV vaccine might be constructed if the various clades were first ranked according to their relative importance. To establish such a ranking the following issues were considered, current prevalence of each clade, the rate at which each clade is increasing and the capacity of various regions of the world to cope with the HIV pandemic (Figures 1 and 2). These criteria produced the following ranking, Clade $E \ge \text{clade } A > \text{clade } C > \text{clade } B > \text{clade } D > \text{other clades. Clades } E \text{ and } A \text{ were}$ considered to almost equal since they are very similar except in their envelope protein sequences, which differ considerably.

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Another advantage of synthesising a designed sequence is that it is possible to incorporate degenerate sequences into their design. In the case of HIV, this means that more than one amino acid can be included at various positions to improve the ability of the vaccine to cater for the various HIV clades and isolates. Coverage is improved because mutations in different HIV clades and also in individual isolate sequences, while mostly destroying specific T cell epitopes, can result in the formation of new potentially useful epitopes nearby (Goulder et al., 1997). Incorporating degenerate amino acid sequences, however, also means that more than one construct must be made and mixed together. The number of constructs required depends on the frequency with which mutations are incorporated into the design. While this approach requires the construction of additional constructs, these constructs can be prepared from the same set of degenerate long oligonucleotides, significantly reducing the cost of providing such considerable interclade coverage.

A set of degeneracy rules was developed for the incorporation of amino acid mutations into the design which meant that a maximum of eight constructs would be required so that theoretically all combinations were present, as follows: 1) Two amino acids at three positions (or less) within any group of nine amino acids (i.e., present in a CTL epitope); 2) Three amino acids at one position and two at another (or not) within any group of nine amino acids; 3) Four amino acids at one position and two at another (or not) within any group of nine amino acids. The reason why these rules were applied to nine amino acids (the average CTL epitope size) and not to larger stretches of amino acid sequence to cater for class II restricted epitopes, is because class II-restricted epitopes generally have a core sequence of nine amino acids in the middle which bind specifically to class II MHC molecules with the extra flanking sequences stabilising binding, by associating with either side of class II MHC antigens in a largely sequence independent manner (Brown et al., 1993).

Using the HIV clade ranking described above, the amino acid degeneracy rules and in some situations the similarity between amino acids, a degenerate consensus protein sequence was designed for each HIV protein using the consensus protein sequences for each HIV clade compiled by the Los Alamos HIV sequence database (Figures 3-11) (HIV Molecular Immunology Database, 1997). It is important to note that in some situations the order with which each of the above design criteria was applied was altered. Each time this 20 was done the primary goal however was to increase the ability of the Savine to cater for interclade differences. Two isolate sequences, GenBank accession U51189 and U46016, for clade E and clade C, respectively, were used when a consensus sequence for some HIV proteins from these two clades was unavailable (Gao et al., 1996; Salminen et al., 1996). The design of a consensus sequence for the hypervariable regions of the HIV envelope protein and in some cases between these regions (hypervariable regions 1-2 and 3-5) was difficult and so these regions were excluded from the vaccine design.

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Once a degenerate consensus sequence was designed for each HIV protein, an approach was then determined for incorporating all the protein sequences safely into the vaccine. One convenient approach to ensure that a vaccine will be safe is to systematically 30 fragment and randomly rearrange the protein sequences together thus abrogating or otherwise altering their structure and function. The protein sequences still have to be immunologically functional however, meaning that the process used to fragment the

sequences should not destroy potential epitopes. To decide on the best approach for systematically fragmenting protein sequences, the main criteria used was the size of T epitopes and their processing requirements. Class I-restricted T cell epitopes are 8-10 amino acids long and generally require 2-3 natural flanking amino acids to ensure their efficient processing and presentation if placed next to unnatural flanking residues (Del Val et al., 1991; Thomson et al., 1995). Class II-restricted T cell epitopes range between 12-25 amino acids long and do appear to require natural flanking residues for processing however, it is difficult to rule out a role for natural flanking residues in all cases due to the complexity of their processing pathways (Thomson et al., 1998). Also class II-restricted epitopes despite being larger than CTL epitopes generally have a core sequence of 9-10 amino acids, which binds to MHC molecules in a sequence specific fashion. Thus, based on current knowledge, it was decided that an advantageous approach was to overlap the fragments by at least 15 amino acids to ensure that potential epitopes which might lie across fragment boundaries are not lost and to ensure that CTL epitopes near fragment boundaries, that are placed beside or near inhibitory amino acids in adjacent fragments, are processed efficiently. In deciding the optimal fragment size, the main criteria used were that size had to be small enough to cause the maximum disruption to the structure and function of proteins but large enough to cover the sequence information as efficiently as possible without any further unnecessary duplication. Based on these criteria the fragments would be twice the overlap size, in this case 30 amino acids long.

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The designed degenerate protein sequences were then separated into fragments 30 amino acid long and overlapping by fifteen amino acids. Two alanine amino acids were also added to the start and end of the first and last fragment for each protein or envelop protein segment to ensure these fragments were not placed directly adjacent to amino acids capable of blocking epitope processing (Del Val et al., 1991). The next step was to reverse translate each protein sequence back into DNA. Duplicating DNA sequences was avoided when constructing DNA sequences encoding a tandem repeat of identical or homologous amino acid sequences to maximise expression of the Savine. In this regard, the first and second most commonly used mammalian codons (shown in Figure 12) were assigned to amino acids in these repeat regions, wherein a first codon was used to encode an amino acid in one of the repeated sequences and wherein a second but synonymous codon was used for the other repeated sequence (e.g., see the gag HIV protein in Figure 13). To cater

for the designed amino acid mutations more than one base was assigned to some positions using the IUPAC DNA codes without exceeding more than three base variations (eight possible combinations) in any group of 27 bases (Figure 12). Where a particular combination of amino acids could not be incorporated, because too many degenerate bases would be required, some or all of the amino acid degeneracy was removed according to the protein consensus design rules outlined above. Also the degenerate codons were checked to determine if they could encode a stop codon, if stop codons could not be avoided then the amino acid degeneracy was also simplified again according to the protein consensus design rules outlined above.

The designed DNA segments were then scrambled randomly and joined to create twenty-two subcassettes approximately 840 bp in size. Extra DNA sequences incorporating sites for one of the cohesive restriction enzymes XbaI, SpeI, AvrII or NheI and 3 additional base pairs (to cater for premature Taq polymerase termination) were then added to each end of each subcassette (Figure 14). Some of these extra DNA sequences also contained, the cohesive restriction sites for SalI or XhoI, Kozak signal sequences and start or stop codons to enable the subcassettes to be joined and expressed either as three large cassettes or one full length protein (Figures 14 and 15).

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In designing the HIV Savine one issue that required investigation was whether such a large DNA molecule would be fully expressed and whether epitopes encoded near the end of the molecule would be efficiently presented to the immune system. The inventors also wished to show that mixing two or more degenerate Savine constructs together could induce T cell responses that recognise mutated sequences. To examine both issues DNA coding for a degenerate murine influenza nucleoprotein CTL epitope, NP365-373, which differs by two amino acids at positions 71 and 72 in influenza strain A/PR/8/34 compared to the A/NT/60/68strain and restricted by H2-Db, was inserted before the last stop codon at the end of the HIV Savine design (Figure 15). An important and unusual characteristic of both of these naturally occurring NP365-373 sequences, which enabled the present inventors to examine the effectiveness of incorporating mutated sequences, is that they generate CTL responses which do not cross react with the alternate sequence (Townsend et. al., 1986). This is an unusual characteristic because epitopes not destroyed by mutation usually induce CTL responses that cross-react.

Up to ten long oligonucleotides up to 100 bases long and two short amplification oligonucleotides were synthesised to enable construction of each subcassette (Life Technologies). In designing each oligonucleotide the 3' end and in most cases also the 5' end had to be either a 'c' or a 'g' to ensure efficient extension during PCR splicing. The overlap region for each long oligonucleotide was designed to be at least 16 bp with approximately 50% G/C content. Also oligonucleotide overlaps were not placed where degenerate DNA bases coded for degenerate amino acids to avoid splicing difficulties later. Where this was too difficult some degenerate bases were removed according to the protein consensus design rules outlined above and indicated in Figure 12. Figure 16 shows an example of the oligonucleotides design for each subcassette.

Construction of the HIV Savine

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Five of each group of ten designed oligonucleotides were spliced together using stepwise asymmetric PCR (Sandhu et al., 1992) and Splicing by Overlap Extension (SOEing) (Figure 17a). Each subcassette was then PCR amplified, cloned into pBluescript™ II KS⁻ using BamHI/EcoRI and 16 individual clones sequenced. Mutations. deletions and insertions were present in the large majority of the clones for each subcassette, despite acrylamide gel purification of the long oligonucleotides. In order to construct a functional Savine with minimal mutations, two clones for each subcassette with no insertions or deletions and hence a complete open reading frame and with minimal numbers of non-designed mutations, were selected from the sixteen available. The subcassettes were then excised from their plasmids and joined by stepwise PCR-amplified ligation using the polymerase blend ElongaseTM (Life Technology), T4 DNA ligase and the cohesive restriction enzymes Xbal/Spel/AvrII/NheI, to generate two copies of cassettes A, B and C as outlined in Figure 14 and shown in Figure 17b. Predicted sequences for these 25 cassettes are shown in Figure 30. Each cassette was then reamplified by PCR with Elongase™, cloned into pBluescript™ II KS- and 3 of the resulting plasmid clones sequenced using 12 of the 36 sequencing primers designed to cover the full length construct. Clones with minimal or no further mutations were selected for transfer into plasmids for DNA vaccination or used to make recombinant poxviruses. A summary of the 30 number of designed and non-designed mutations in each Savine construct is presented in Table 1.

TABLE 1
Summary of mutations

| Corsinct | No. 225 | Namber of countions | | | | |
|-------------|---------|---------------------|-------------------------|-----------------------|--------------------|--|
| | | Designed | Expected in 2 clones | Actual in 2 clones | Non-designed | |
| Cassette A | 1896 | 249 | 124 | 107 | 5 (AC1), 8 (AC2) | |
| Cassette B | 1184 | 260 | 130 | 124 | 11 (BC1), 4 (BC2) | |
| Cassette C | 1969 | 276 | 138 | 121 | 10 (CC1), 14 (CC2) | |
| Full length | 5742 | 785 | 392 | 352 | 26 (FL1), 26 (FL2) | |

Summary of the mutations present in the two full-length clones constructed as determined by sequencing. Includes the number of mutations designed, expected and actually present in the 2 clones and the number of non-designed mutations in each cassette and full-length clone.

HIV Savine DNA vaccines and Recombinant Vaccinia viruses

To test the immunological effectiveness of the HIV Savine constructs the cassette sequences were transferred into DNA vaccine and poxvirus vectors. These vectors when used either separately in immunological assays described below or together in a 'prime-boost' protocol which has been shown previously to generate strong T cell responses in vivo (Kent et al., 1997).

DNA Vaccination plasmids were constructed by excising the cassettes from the selected plasmid clones with Xbal/XhoI (cassette A) or Xbal/SalI (cassettes B and C) and ligating them into pDNAVacc cut with Xbal/XhoI to create pDVAC1, pDVAC2, pDVBC1, pDVBC2, pDVCC1, pDVCC2, respectively (Figure 18a). These plasmids were then further modified by cloning into their XbaI site a DNA fragment excised using Xbal/AvrII from pTUMERA2 and encoding a synthetic endoplasmic reticulum (ER) signal sequence from the Adenovirus E1A protein (Persson et al., 1980) (Figure 18a). ER signal sequences have been shown previously to enhance the presentation of both CTL and T helper epitopes in vivo (Ishioka, G.Y., 1999; Thomson et al., 1998). The plasmids pDVERAC1, pDVERBC1, pDVERCC1 and pDVERAC2, pDVERBC2, pDVERCC2 were then mixed

together to create, plasmid pool 1 and pool 2 respectively. Each plasmid pool collectively encodes one copy of the designed full-length HTV Savine.

Plasmids to generate recombinant Vaccinia viruses which express HIV Savine sequences were constructed by excising the various HIV Savine cassettes from the selected plasmid clones using BamHI/XhoI (cassette A) or BamHI/SaII (cassettes B and C) and cloned into the marker rescue plasmid, pTK7.5, cleaved with BamHI/SalI. These pTK7.5derived plasmids were then used to generate recombinant Vaccinia viruses by marker rescue recombination using established protocols (Boyle et al., 1985) to generate VV-AC1, VV-AC2, VV-BC1, VV-BC2, VV-CC1 and VV-CC2 (Figure 18b).

Two further DNA vaccine plasmids were constructed each encoding a version of the full length HIV Savine (Figure 18c). Briefly, the two versions of cassette B were excised with XhoI and cloned into the corresponding selected plasmid clones containing cassette A sequences that were cut with XhoI/SaII to generate pBSAB1 and pBSAB2 respectively. The joined A/B cassettes in pBSAB1 and pBSAB2 were excised with 15 Xbal/XhoI and cloned into pDVCC1 and pDVCC2, respectively, and cleaved with Xbal/XhoI to generate pDVFL1 and pDVFL2. These were then further modified to contain an ER signal sequence using the same cloning strategy as outlined in figure 18a.

Restimulation of HIV specific lymphocytes from HIV infected patients

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The present inventors examined the capacity of the HIV Savine to restimulate HIV-specific polyclonal CTL responses from HIV-infected patients. PBMCs from three different patients were restimulated in vitro with two HIV Savine Vaccinia virus pools (Pool 1 included VV-AC1 and VV-BC1; Pool 2 included VV-AC2, VV-BC2 and VV-CC2) then used in CTL lysis assays against LCLs infected either with one of the Savine Vaccinia virus pools or Vaccinia viruses which express gag, env or pol. Figure 19 clearly shows, 25 that in all three assays, both HIV Savine viral pools restimulated HIV-specific CTL responses which could recognise targets expressing whole natural HIV antigens and not targets which were uninfected or infected with the control Vaccinia virus. Furthermore, in all three cases, both pools restimulated responses that recognised all three natural HIV antigens. This result suggests that the combined Savine constructs will provide broader 30 immunological coverage than single antigen based vaccine approaches. The level of lysis in each case of targets infected with Savine viral pools was significantly higher than the

lysis recorded for any other infected target. This probably reflects the combined CTL responses to gag, pol, and env plus other HIV antigens not analysed here but whose sequences are also incorporated into the Savine constructs.

CTL recognition of each HIV antigen is largely controlled by each patient's HLA background hence the pattern of CTL lysis for whole HIV antigens is different in each patient. Interestingly, this CTL lysis pattern did not change when the second Savine Vaccinia virus pool was used for CTL restimulation. In these assays, therefore, the inventors were unable to demonstrate clear differences between pools 1 and 2, despite pool 1 lacking a Vaccinia virus expressing cassette CC1 and despite the many amino acid differences between the A and B cassettes in each pool (see table 1).

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From the foregoing, the present inventors have developed a novel vaccine/therapeutic strategy. In one embodiment, pathogen or cancer protein sequences are systemically fragmented, reverse translated back into DNA, rearranged randomly then joined back together. The designed synthetic DNA sequence is then constructed using long oligonucleotides and can be transferred into a range of delivery vectors. The vaccine vectors used here were DNA vaccine plasmids and recombinant poxvirus vectors which have been previously shown to elicit strong T cell responses when used together in a 'prime-boost' protocol (Kent et al., 1997). An important advantage of scrambled antigen vaccines or 'Savines' is that the amount of starting sequence information for the design can be easily expanded to include the majority of the protein sequences from a pathogen or for cancer, thereby providing the maximum possible vaccine or therapy coverage for a given population.

An embodiment of the systematic fragmentation approach described herein was based on the size and processing requirements for T cell epitopes and was designed to cause maximal disruption to the structure and function of protein sequences. This fragmentation approach ensures that the maximum possible range of T cell epitopes will be present from any incorporated protein sequence without the protein being functional and able to compromise vaccine safety

Another important advantage of Savines is that consensus protein sequences can be used for their design. This feature is only applicable when the design needs to cater for pathogen or cancer antigens whose sequence varies considerably. HIV is a highly

mutagenic virus, hence this feature was utilised extensively to design a vaccine which has the potential to cover not only field isolates of HIV but also the major HIV clades involved in the current HIV pandemic. To construct the HIV Savine, one set of long oligonucleotides was synthesised, which included degenerate bases in such a way that 8 constructs are theoretically required for the vaccine to contain all combinations in any stretch of 9 amino acids. The inventors believe that this approach can be improved for the following reasons: 1) While degenerate bases should be theoretically equally represented, in practice some degenerate bases were biased towards one base or the other, leading to a lower than expected frequency of the designed mutations in the two full length HIV Savines which were constructed (see Table 1). 2) Only sequence combinations actually present in the HIV clade consensus sequences are required to get full clade coverage, hence the number of full length constructs needed could be reduced. To reduce the number of constructs however, separate sets of long oligonucleotides would have to be synthesised, significantly increasing the cost, time and effort required to generate a vaccine capable of such considerable vaccine coverage.

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A significant problem during the construction of the HIV Savine synthetic DNA sequence was the incorporation of non-designed mutations. The most serious types of mutations were insertions, deletions or those giving rise to stop codons, all of which change the frame of the synthesised sequences and/or caused premature truncation of the Savine proteins. These types of mutation were removed during construction of the HIV Savines by sequencing multiple clones after subcassette and cassette construction and selecting functional clones. The major source of these non-designed mutations was in the long oligonucleotides used for Savine synthesis, despite their gel purification. This problem could be reduced by making the initial subcassettes smaller thereby reducing the possibility of corrupted oligonucleotides being incorporated into each subcassette clone. The second major cause of non-designed mutations was the large number of PCR cycles required for the PCR and ligation-mediated joining of the subcassettes. Including extra sequencing and clone selection steps during the subcassette joining process should help to reduce the frequency of non-designed mutations in future constructs. Finally, another method that could help reduce the frequency of such mutations at all stages is to use resolvase treatment. Resolvases are bacteriophage-encoded endonucleases which recognise disruptions to double stranded DNA and are primarily used by bacteriophages to resolve

Holliday junctions (Mizuuchi, 1982; Youil et al., 1995). T7 endonuclease I has already been used by the present inventors in synthetic DNA constructions to recognise mutations and cleave corrupted dsDNA to allow gel purification of correct sequences. Cleavage of corrupted sequences occurs because after a simple denaturing and hybridisation step mutated DNA hybridises to correct DNA sequences and results in a mispairing of DNA bases which is able to be recognised by the resolvase. This method resulted in a 50% reduction in the frequency of errors. Further optimisation of this method and the use of a thermostable version of this type of enzyme could further reduce the frequency of errors during long Savine construction.

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Two pools of Vaccinia viruses expressing Savine cassettes were both shown to restimulate HIV-specific responses from three different patients infected with B clade HIV viruses. These results provide a clear indication that the HIV Savine should provide broad coverage of the population because each patient had a different HLA pattern yet both pools were able to restimulate HIV-specific CTL responses in all three patients against all three 15 natural HIV proteins tested. Also, both pools were shown to restimulate virtually identical CTL patterns in all three patients. This result was unexpected because some responses should have been lost or gained due to the amino acid differences between the two pools and because Pool 1 is only capable of expressing 2/3 of the full length HIV Savine. There are two suggested reasons why the pattern of CTL lysis was not altered between the two 20 viral pools. Firstly, the sequences in the Savine constructs are nearly all duplicated because the fragment sequences overlap. Hence the loss of a third of the Savine may not have excluded sufficient T cell epitopes for differences to be detected in only three patient samples against only three HIV proteins. Secondly, while mutations often destroy T cell epitopes, if they remain functional, then the CTL they generate frequently can recognise alternate epitope sequences. Taken together this finding indirectly suggests that combining only two Savine constructs may provide robust multiclade coverage. Further experiments are being carried out to directly examine the capacity of the HIV Savine to stimulate CTL generated by different strains of HIV virus. The capacity of the two HIV-1 Savine Vaccinia vector pools to stimulate CD4+ T cell HIV-1 specific responses from infected patients was also tested (Figure 20). Both patients showed significant proliferation of CD4+ T cells although both pools did not show consistent patterns suggesting that the two pools may provide wider vaccine coverage than using either pool independently.

The present inventors have generated a novel vaccine strategy, which has been used to generate what the inventors believe to be the most effective HIV candidate vaccine to date. The inventors have used this vaccine to immunise naive mice. Figure 21 shows conclusively that the HIV-1 Savine described above can generate a Gag and Nef CTL response in naïve mice. It should be noted, however, that the Nef CTL epitope appeared to exist only in Pool 1 since it was not restimulated by Pool 2. This is further proof of the utility of combining HIV-1 Savine Pool 1 and Pool 2 components together to provide broader vaccine coverage.

The HIV-1 Savine Vaccinia vectors have also been used to restimulate in vivo HIV-1 responses in pre-immune M. nemestrina monkeys. These experiments (Figure 22) showed, by INF-γ ELISPOT and CD69 expression on both CD4 and CD8 T cells, that the ability of the HIV-1 SAVINE to restimulate HIV-1 specific responses in vivo is equivalent or perhaps better than another HIV-1 candidate vaccine.

This is a generic strategy able to be applied to many other human infections or cancers where T-cell responses are considered to be important for protection or recovery. With this in mind the inventors have begun constructing Savines for melanoma, cervical cancer and Hepatitis C. In the case of melanoma, the majority of the currently identified melanoma antigens have been divided into two groups, one containing antigens associated with melanoma and one containing differentiation antigens from melanocytes, which are often upregulated in melanomas. Two Savine constructs are presently being constructed to cater for these two groups. The reason for making the distinction is that treatment of melanoma might first proceed using the Savine that incorporates fragments of melanoma specific antigens only. If this Savine fails to control some metastases then the less specific Savine containing the melanocyte-specific antigens can then be used. It is important to point out that other cancers also express many of the antigens specific to melanomas e.g., testicular and breast cancers. Hence the melanoma specific Savine may have therapeutic benefits for other cancers.

A small Savine is also being constructed for cervical cancer. This Savine will contain two antigens, E6 and E7, from two strains of human papilloma virus (HPV), HPV
16 and HPV-18, directly linked with causing the majority of cervical cancers worldwide.

There is a large number of sequence differences in these two antigens between the two

strains which would normally require two Savines to be constructed. However since this Savine is small, the antigen fragments from both strains are being scrambled together. While it is normally better for the Savine approach to include all or a majority of the antigens from a virus, in this case only E6 and E7 are expressed during viral latency or in cervical carcinomas. Hence in the interests of simplicity, the rest of the HPV genome will not be included although all HPV antigens would be desirable in a Savine against genital warts.

Two Savines have also been constructed for two strains of hepatitis C, a major cause of liver disease in the world. Hepatitis C is similar to HIV in the requirements for a vaccine or therapeutic. However, the major hepatitis C strains share significantly lower homology, 69-79%, with one another than do the various HIV clades. To cater for this the inventors have decided to construct two separate constructs to cater for the two major strains present in Australia, types 1 aand 3a, which together cause approximately 80-95% of hepatitis C infections in this country. Both constructs will be approximately the same size as the HIV Savine but will be blended together into a single vaccine or therapy.

Overall it is believed that the Savine vaccine strategy is a generic technology likely to be applied to a wide range of human diseases. It is also believed that because it is not necessary to characterise each antigen, this technology will be actively applied to animal vaccines as well where research into vaccines or therapies is often inhibited by the lack of specific reagents, modest research budgets and poor returns on animal vaccines.

EXAMPLE 2

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Hepatitis C Savine

Synthetic immunomodulatory molecules have also been designed for treating Hepatitis C. In one example, the algorithm of Figure 25 was applied to a consensus polyprotein sequence of Hepatitis C 1a to facilitate its segmentation into overlapping segments (30 aa segments overlapping by 15 aa), the rearrangement of these segments into a scrambled order and the output of Savine nucleic acid and amino acid sequences, as shown in Figure 26. Exemplary DNA cassettes (A, B and C) are also shown in Figure 26, which contain suitable restriction enzyme sites at their ends to facilitate their joining into a single expressible open reading frame.

EXAMPLE 3

Melanoma Savine

The algorithm of Figure 25 was also applied to melanocyte differentiation antigens (gp100, MART, TRP-1, Tyros, Trp-2, MC1R, MUC1F and MUC1R) and to melanoma specific antigens (BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b and LAGE1), as shown in Figure 27, to provide separate Savine nucleic acid and amino acid sequences for treating or preventing melanoma.

EXAMPLE 4

Resolvase Repair Experiment

A resolvase can be used advantageously to repair errors in polynucleotides. The following procedure outlines resolvase repair of a synthetic 340 bp fragment in which DNA errors were common.

Method

The 340 bp fragment was PCR amplified and gel purified on a 4% agarose gel. After spin purifying, 10ul of the eluate corresponding to approximately 100 ng was subjected to the resolvase repair treatment. The rest of the DNA sample was stored for later cloning as the untreated control.

2 μL of 10xPCR buffer, 2 μL of 20 mM MgCl₂ and 6 μL of MilliQ™ water (MQW) and Taq DNA polymerase were added to the 10 μL DNA sample. The mixture was subjected to the following thermal profile; 95°C for 5min, 65°C for 30min, cooled and held at 37°C. Five μL of 10xT7 endonuclease I buffer, 8 μL of 1/50 μL of T7endoI enzyme stock and 17 μL of MQW were added, mixed and incubated for 30 min. Loading buffer was added to the sample and the sample was electrophoresed on a 4% agarose gel. A faint band corresponding to the full length fragment was excised and subjected to 15 further cycles of PCR. The amplified fragment was agarose gel purified and, along with the untreated DNA sample, cloned into pBluescript. Eleven plasmid clones for each DNA sample were sequenced and the number and type of errors compared (see table)

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Buffers were as follows:

10x T7endonuclease buffer

2.5ml 1M TRIS pH7.8, 0.5ml 1M MgCl₂, 25 μ L 1 M DTT, 50 μ L 10mg/mL BSA, 2 mL MQW made up to a total of 5 mL.

5 T7 endonuclease I stock

Concentrated sample of enzyme prepared by, and obtained from, Jeff Babon (St Vincent's Hospital) was diluted 1/50 using the following dilution buffer: 50 μ L 1 M TRIS pH7.8, 0.1 μ L 1M EDTA pH8, 5 μ L 100 mM glutathione, 50 μ L 10mg/mL BSA, 2.3 mL MQW, 2.5 mL glycerol made up to a total of 5 mL.

10 Results

The results are summarised in Tables 2 and 3.

TABLE 2

| Total Leros | | | | |
|---------------------|---------------------|--|--|--|
| Universed | Resolvane medical | | | |
| A/T to $G/C = 6$ | A/T to G/C = 1 | | | |
| G/C to A/T = 12 | G/C to $A/T = 7$ | | | |
| A/T to deletion = 1 | A/T to deletion = 1 | | | |
| G/C to deletion = 6 | G/C to deletion = 3 | | | |

TABLE 3

| Chae summary | | | | |
|--------------------------|--------------------------|--|--|--|
| Uttorated | Resolvine remed | | | |
| 6/11 contained deletions | 3/11 contained deletions | | | |
| 9/11 contained mutations | 7/11 contained mutations | | | |

| Cloue shinnery | | | | |
|----------------|-------------------|--|--|--|
| Universed | Resolvace breated | | | |
| 2/11 correct | 3/11 correct | | | |

Discussion/Conclusion

While overall the number of correct clones obtained was not significantly different, there was a significant difference in the level of errors. This reduction in errors becomes more significant as greater numbers of long oligonucleotides are joined into the one construct *i.e.*, increasing the difference between untreated *versus* treated samples in the chance of obtaining a correct clone. It is believed that combining another resolvase such as T4 endonuclease VII may further enhance repair or increase the bias against errors.

Importantly, this experiment was not optimised e.g., by using proofreading PCR enzymes or optimised conditions. Finally if the repair reaction is carried out during normal PCR, for example, by including a thermostable resolvase, it is believed that amplification of already damaged long oligonucleotides, and the normal accumulation of PCR induced errors, even using error reading polymerases during PCR, could be reduced significantly. The repair of damaged long oligonucleotides is particularly important for synthesis of long DNA fragment such as in Savines because, while the rate of long oligonucleotide damage is typically <5%, after joining 10 oligonucleotides, the error rate approaches 50%. This is true even using the best proofreading PCR enzymes because these enzymes do not verify the sequence integrity using correct oligonucleotide templates that exist as a significant majority (95%) in a joining reaction.

The disclosure of every patent, patent application, and publication cited herein is incorporated herein by reference in its entirety.

The citation of any reference herein should not be construed as an admission that such reference is available as "Prior Art" to the instant application

Throughout the specification the aim has been to describe the preferred embodiments of the invention without limiting the invention to any one embodiment or specific collection of features. Those of skill in the art will therefore appreciate that, in

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light of the instant disclosure, various modifications and changes can be made in the particular embodiments exemplified without departing from the scope of the present invention. All such modifications and changes are intended to be included within the scope of the appended claims.

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WO 01/090197

WHAT IS CLAIMED IS:

- 1. A synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide.
- 2. The synthetic polypeptide of claim 1, consisting essentially of different segments of a single parent polypeptide.
- 3. The synthetic polypeptide of claim 1, consisting essentially of different segments of a plurality of different parent polypeptides.
- 4. The synthetic polypeptide of claim 1, wherein the segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to their linkage in said at least one parent polypeptide.
- 5. The synthetic polypeptide of claim 4, wherein the segments in said synthetic polypeptide are randomly rearranged relative to their order or arrangement in said at least one parent polypeptide.
- 6. The synthetic polypeptide of claim 1, wherein the size of an individual segment is at least 4 amino acids.
- 7. The synthetic polypeptide of claim 6, wherein the size of an individual segment is from about 20 to about 60 amino acids.
- 8. The synthetic polypeptide of claim 7, wherein the size of an individual segment is about 30 amino acids.
- 9. The synthetic polypeptide of claim 7, comprising at least 30% of the parent polypeptide sequence.
- 10. The synthetic polypeptide of claim 1, wherein at least one of said segments comprises partial sequence identity or homology to one or more other said segments.
- 11. The synthetic polypeptide of claim 10, wherein the sequence identity or homology is contained at one or both ends of an individual segment.

- 12. The synthetic polypeptide of claim 11, wherein one or both ends of said segment comprises at least 4 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments.
- 13. The synthetic polypeptide of claim 10, wherein the size of an individual segment is about twice the size of the sequence that is identical or homologous to the or each other said segment.
- 14. The synthetic polypeptide of claim 13, wherein the size of an individual segment is about 30 amino acids and the size of the sequence that is identical or homologous to the or each other said segment is about 15 amino acids.
- 15. The synthetic polypeptide of claim 1, wherein an optional spacer is interposed between some or all of the segments.
- 16. The synthetic polypeptide of claim 15, wherein the spacer alters proteolytic processing and/or presentation of adjacent segment(s).
- 17. The synthetic polypeptide of claim 16, wherein the spacer comprises at least one neutral amino acid.
- 18. The synthetic polypeptide of claim 16, wherein the spacer comprises at least one alanine residue.
- 19. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is associated with a disease or condition.
- 20. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is selected from a polypeptide of a pathogenic organism, a cancer-associated polypeptide, an autoimmune disease-associated polypeptide, an allergy-associated polypeptide or a variant or derivative of these.
- 21. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is a polypeptide of a virus.
- 22. The synthetic polypeptide of claim 21, wherein the virus is selected from a Human Immunodeficiency Virus (HIV) or a Hepatitis virus.
- 23. The synthetic polypeptide of claim 22, wherein the virus is a Human Immunodeficiency Virus (HIV) and the at least one parent polypeptide is selected from env, gag, pol, vif, vpr, tat, rev, vpu and nef, or a combination thereof.

- 24. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is a cancer-associated polypeptide.
- 25. The synthetic polypeptide of claim 24, wherein the cancer is melanoma.
- 26. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanocyte differentiation antigen.
- 27. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanocyte differentiation antigen selected from gp100, MART, TRP-1, Tyros, TRP2, MC1R, MUC1F, MUC1R or a combination thereof.
- 28. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanoma-specific antigen.
- 29. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanoma-specific antigen selected from BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b, LAGE1 or a combination thereof.
- 30. A synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide.
- 31. A method for producing the synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, said method comprising:
 - linking together in the same reading frame a plurality of nucleic acid sequences encoding different segments of the at least one parent polypeptide to form a synthetic polynucleotide whose sequence encodes said segments linked together in a different relationship relative to their linkage in the at least one parent polypeptide.
- 32. The method of claim 31, further comprising fragmenting the sequence of a respective parent polypeptide into fragments and linking said fragments together in a different relationship relative to their linkage in a respective parent polypeptide sequence.

- 33. The method of claim 32, wherein the fragments are randomly linked together.
- 34. The method of claim 31, further comprising reverse translating the sequence of a respective parent polypeptide or a segment thereof to provide a nucleic acid sequence encoding said parent polypeptide or said segment.
- 35. The method of claim 34, wherein an amino acid of a respective parent polypeptide sequence is reverse translated to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.
- 36. The method of claim 35, wherein an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.
- 37. The method of claim 35, wherein an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence selected from a palindromic sequence or a duplicated sequence, which is refractory to the execution of a task selected from cloning or sequencing.
- 38. The method of claim 31, further comprising linking a spacer oligonucleotide encoding at least one spacer residue between segment-encoding nucleic acids.
- 39. The method of claim 38, wherein spacer oligonucleotide encodes 2 to 3 spacer residues.
- 40. The method of claim 38 or claim 39, wherein the spacer residue is a neutral amino acid.
- 41. The method of claim 38 or claim 39, wherein the spacer residue is alanine.
- 42. The method of claim 31, further comprising linking in the same reading frame as other segment-containing nucleic acid sequences at least one variant nucleic acid sequence which encodes a variant segment having a homologous but not identical amino acid sequence relative to other encoded segments.

- 43. The method of claim 42, wherein the variant segment comprises conserved and/or non-conserved amino acid differences relative to one or more other encoded segments.
- 44. The method of claim 43, wherein the differences correspond to sequence polymorphisms.
- 45. The method of claim 44, wherein degenerate bases are designed or built in to the at least one variant nucleic acid sequence to give rise to all desired homologous sequences.
- 46. The method of claim 31, further comprising optimising the codon composition of the synthetic polynucleotide such that it is translated efficiently by a host cell.
- 47. A synthetic construct comprising a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said synthetic polynucleotide is operably linked to a regulatory polynucleotide.
- 48. The synthetic construct of claim 47, further including a nucleic acid sequence encoding an immunostimulatory molecule.
- 49. The synthetic construct of claim 48, wherein the immunostimulatory molecule comprises a domain of an invasin protein (Inv).
- 50. The synthetic construct of claim 48, wherein the immunostimulatory molecule comprises the sequence set forth in SEQ ID NO: 1467 or an immune stimulatory homologue thereof.
- 51. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a T cell co-stimulatory molecule.
- 52. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a T cell co-stimulatory molecule selected from a B7 molecule or an ICAM molecule.
- 53. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a B7 molecule or a biologically active fragment thereof, or a variant or derivative of these.

- 54. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a cytokine selected from an interleukin, a lymphokine, tumour necrosis factor or an interferon.
- 55. The synthetic construct of claim 48, wherein the immunostimulatory molecule is an immunomodulatory oligonucleotide.
- 56. An immunopotentiating composition, comprising an immunopotentiating agent selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30 or the synthetic construct of claim 47, together with a pharmaceutically acceptable carrier.
- 57. The composition of claim 56, further comprising an adjuvant.
- 58. A method for modulating an immune response, which response is preferably directed against a pathogen or a cancer, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30, the synthetic construct of claim 47, or the composition of claim 56.
- 59. A method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30, the synthetic construct of claim 47, or the composition of claim 56.
- 60. A computer program product for designing the sequence of a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, said program product comprising:
 - code that receives as input the sequence of said at least one parent polypeptide;
 - code that fragments the sequence of a respective parent polypeptide into fragments;
 - code that links together said fragments in a different relationship relative to their linkage in said parent polypeptide sequence; and

- a computer readable medium that stores the codes.
- 61. The computer program product of claim 60, further comprising code that randomly rearranges said fragments.
- 62. The computer program product of claim 60, further comprising code that links the sequence of a spacer residue to the sequence of said at least one parent polypeptide or to said fragments.
- 63. A computer program product for designing the sequence of a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, comprising:
 - code that receives as input the sequence of at least one parent polypeptide;
 - code that fragments the sequence of a respective parent polypeptide into fragments;
 - code that reverse translates the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment;
 - code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence; and
 - a computer readable medium that stores the codes.
- 64. The computer program product of claim 63, further comprising code that randomly rearranges said nucleic acid sequences.
- 65. The computer program product of claim 64, further comprising code that reverse translates an amino acid of a respective parent polypeptide sequence to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.
- 66. The computer program product of claim 63, further comprising code that reverse translates an amino acid of a respective parent polypeptide sequence to provide a codon

which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.

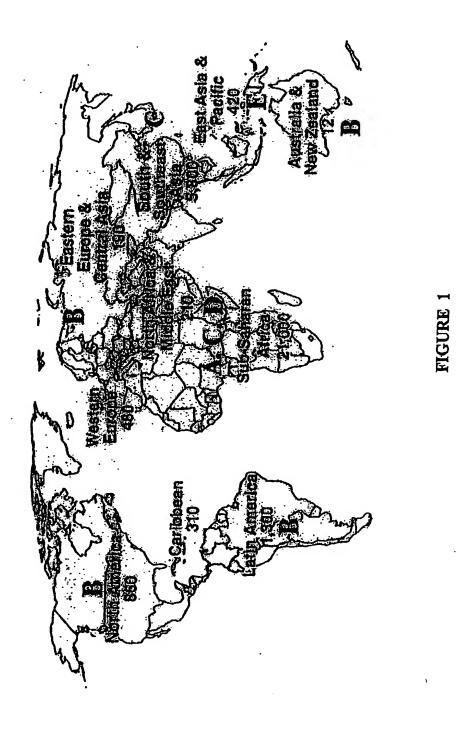
- 67. The computer program product of claim 63, further comprising code that links a spacer oligonucleotide to one or more of said nucleic acid sequences.
- 68. A computer for designing the sequence of a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said computer comprises:
 - (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
 - (b) a working memory for storing instructions for processing said machine-readable data;
 - (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polypeptide sequence; and
 - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence.
- 69. The computer of claim 68, wherein the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking together said fragments in a different relationship relative to their linkage in the sequence of said parent polypeptide.
- 70. The computer of claim 68, wherein the processing of said machine readable data comprises randomly rearranging said fragments.
- 71. The computer of claim 68, wherein the processing of said machine readable data comprises linking the sequence of a spacer residue to the sequence of said at least one parent polypeptide or to said fragments.

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- 72. A computer for designing the sequence of a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said computer comprises:
 - (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
 - (b) a working memory for storing instructions for processing said machine-readable data;
 - (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polynucleotide sequence; and
 - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polynucleotide sequence.
- 73. The computer of claim 72, wherein the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments, reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment and linking together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence.
- 74. The computer of claim 72, wherein the processing of said machine readable data comprises randomly rearranging said nucleic acid sequences.
- 75. The computer of claim 72, wherein the processing of said machine readable data comprises reverse translating an amino acid of a respective parent polypeptide sequence to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.

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76. The computer of claim 72, wherein the processing of said machine readable data comprises reverse translating an amino acid of a respective parent polypeptide sequence to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.

77. The computer of claim 72, wherein the processing of said machine readable data comprises linking a spacer oligonucleotide to one or more of said nucleic acid sequences.



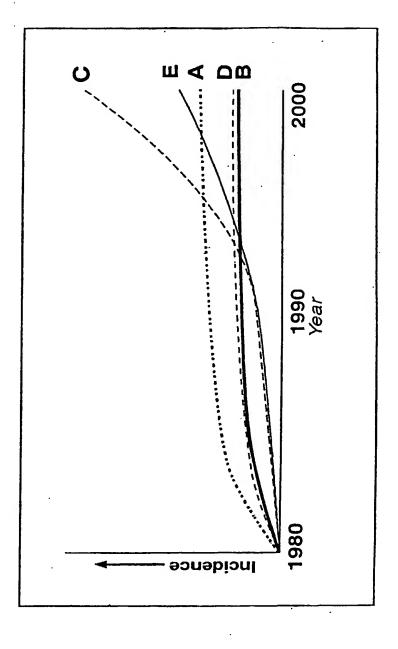


FIGURE 2

| pI | 17 -> /<- nls ->/ / membrane binding ->/ | • |
|-----------------------------|--|------------|
| DESIGNED SEQ | ngarasvisggkidawekirlrpggkkky <u>k</u> mkhlvwasrelerpainpglietaegcoqileqiqsalkt r b ri i <u>s</u> s k g p q | 70 |
| E-ISOLATE | mgarasvi.sggki.dameki.rl.rpggkkkykmkhi.vmasrelerfalmpglletaegcqqlieqi.qstlkt | 70 |
| CONSENSUS-A | mGARaSvLsggkLDawekIrLRPgGkKkYrlKHlvwAsreLerFaLnPslLeTaegcqqimeQlqsalkT | 70 |
| CONSENSUS-B | vgsRlgps-q- | 70 |
| CONSENSUS-C | i-r | 69 |
| CONSENSUS-D CONSENSUS-F | G | 68 70 |
| CONSENSUS-F | | 63 |
| CONSENSUS-H | | 64 |
| CONSENSUS-O | ?T-S?E?LLQEP | 62 |
| CONSENSUS-CP2 | Z??-???????7??????-?????K????D???? | 42 |
| | /<- nls ->/ | |
| DESIGNED SEQ MUTATED AAS | GSEELKSLYNTIATIWCVHQRIEVKDTKEALDKIEKEQKKSQQKTQQAAADT.GSSSKV T R F V D R · V N K N . Q | |
| E-ISOLATE | GSEELKSLYNTIATLMCVHQRIEVKDTKEALDKIEEVQKKSQQKKQQAAADT.GSSSKV | |
| CONSENSUS-A | g?eElkSLfNtvatLycvHqrIdvkDtKeAldkiEeiqnKskqk??????tqqaaA?T.gs?sskv | 126 |
| CONSENSUS-B | -6xy | 128 |
| CONSENSUS-C | -Tr???-e-rB?QkaD?k | 120 |
| CONSENSUS-D | -s?eeee-mEkatDrnQ- | 125 |
| CONSENSUS-F | -SryvELEq?dK | 123 |
| CONSENSUS-G | -T??-??-?-?eeEV-Ka-kn-Q???e7nq- -TQLL-???-?-?-?-????T?DK.????-? | 110 106 |
| CONSENSUS-H CONSENSUS-O | -5??-?N-A1?V-NN-??1?QQ-IQ-LK-V.M?-RKSA-AAKE?RQ? | 106 |
| CONSENSUS-CPZ | 2\$??????V-W-?-?????????-???K??????Q??T-S???G????-???????? | 61 |
| • | p17 \/ p24 | |
| DESIGNED SEQ | SQNYPIVQNAQGQMVHQPLSPRTLNAWVKVIEEKGFNPEVIPMFSALSEGATPQDLNMMLNIVGGH | |
| MUTATED AAS | L AI V AS T T T | |
| E-ISOLATE . | SQNYPIVQNAQGQMVHQPLSPRTLNANVKVIEEKGPNPEVIPMFSALSEGATPQDLNMMLNIVGGH | |
| CONSENSUS-A | ????SqNYPIVQNaqgQm?hQ?lSPrTLnAwVKviEekaFspEVIPmFsaLSEGATpQdLNmMLWiVgGH | 190 |
| CONSENSUS-B | | 194 |
| CONSENSUS-C | TTTT | 185 191 |
| CONSENSUS-D | | 188 |
| CONSENSUS-F CONSENSUS-G | tT | 174 |
| CONSENSUS-H | | 170 |
| CONSENSUS-O | ??VAIAVNIM??Y-I-TAI | 168 |
| CONSENSUS-CPZ | ??????-?-???V?-?-??-?-?-?-TA?- | 107 |
| | AAMOMIKETINEEAAEWDRVHPVHAGPIPPGOMREPRGSDIAGTTSTLQEQIGWMTNNPPIPVGDI | |
| MUTATED AAs | D I VAI ASVE | |
| E-ISOLATE Q | AAMOMLKETINEEAAENDRVHPVHAGPIPPGQMREPRGSDIAGTTSTLQEQIGNMTNNPPIPVGDI | |
| CONSENSUS-A | QAAMQMLKdtINeEAAewDr?HPVhAgPippgQmREPrGSDIAGtTStlqEqigwmTsNPPiPVGdI | 256 |
| | ene- | 261 |
| - | a? | 251 |
| | | 257 |
| | | 255 239 |
| | | 239 |
| | -G-L-VEV?TP??LITQ?-T-R.??-?? | 233 |
| CONSENSUS-O | -G-L-VEV | 160 |
| CUNSENSUS-CPZ | -GAEA | |

FIGURE 3

MHR

->/

/<-

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| | | | | p 2 | 4 \/ | V | 'p2' | V | p 7 | | Zn-m /< | |
|-----------------------------|---------------|------------------|---------------------|-----------------|-----------|-----------|--------------|------------------|------------|-------------|-------------|------------|
| DESIGNED SEC | SILKAI T R | GTGATLEEM P S | MTACQGVGGI | PSHKAR G | VLAEA | MSQA V | .TH.AN | IMMQI | | KGQKR RP | IIKCPN V | ٠ |
| ISOLATE-E | SILKAL | GTGATLEEM | MTACQGVGGI | SHKAR | VLAEAI | ISQA | .QH.AN. | IMMQI | GNP. | KGQTR | . IKCFN | |
| CONSENSUS-A | sILra | Lg?gAtLeE | M TacQgVgg | РдНКАз | VLABA | mSqv. | q???n | ??. iM mQ | rGnf. | rggkr | ?iKCFN | 38 |
| CONSENSUS-B | | | | | | | | | | | | |
| CONSENSUS-C | T | Ps | | -s - | | a. | nn | | -8 | K-p | iv | 38 |
| CONSENSUS-D | tK | P? | | -5 | | a | .tn.s- | ta | | K-prk | :i | 39 |
| CONSENSUS-F | TK- | P | | | | a | .TN? | a | ks | KR- | iv | . 381 |
| CONSENSUS-G | T?- | P | | -? | | A | .SGA | -A.? | K?? | K-P?? | 3 | 361 |
| CONSENSUS-H | ?? | SI | | -?? | | ?. | .TN? | A? | К | KR- | I? | 35: |
| CONSENSUS-O | QK?· | | -V | -T? | ? | -A?AQQ | DLKGGY | TA.VP | QN. | P?R-G | | 351 |
| CONSENSUS-CP | 6 ?K | : | ? | - ? | | -22777 | .?Q?· | VF?- | ?-?G? | ?-? | -? | 262 |
| | P= | | / 5 | | | cds - | | | | | | • |
| | Zn-mot | if ->/ | /<-Zn-n | ocır - | ->/ | p7· (| , . | p1' | \/ | рб | | |
| DESIGNED SEQ | CGKEGHI | ARNCRAPRK | KGCWKCGKEC | номко | CTB | ROANE | LGKIWPS | NKG.RPC | NPPQ: | SKP | | |
| MUTATED AAs | | IK | R | | | | | H. | L | R | | |
| ISOLATE-E | CGKBGHL | ARNCRAPRK | KGCWKCGKEG | НОМКОО | T.E. | ROANF | s LGKIWPS | NKG . RPG | NFPQS | SKP | | |
| CONSENSUS-A | CG/kEGH | larncrapri | KkGCwKCgkE | GHQmKd | CT.?e | . rQANI | ?lgkiwp | SSKG.RP | gNFpC | sRp | | 443 |
| CONSENSUS-B | | | | | | | | | | | | 453 |
| CONSENSUS-C | | | ?- | | | | | | | | | 439 |
| CONSENSUS-D | | | | | | | | | | | | 449 |
| CONSENSUS-F | | | ?r- | | | | | | | | | 445 |
| CONSENSUS-G | | | | | | | | | | | | 414 |
| CONSENSUS-H CONSENSUS-O | | | ?~-Q- | | | | | | | | | 406 |
| CONSENSUS-CPZ | | | | | | | | | | | | 411 306 |
| | • | pr bindin | 9 | | | | | | vpr | bindi | ing | p6 |
| | | /<>/ | | | | | | | | | ter | minus |
| | | | | | minor | | | nor) . \/ | | <> | • | (80%) |
| DESIGNED SEQ MUTATED AAS | 1 | SPTAPPAB | NF.G | GEETT | . PS | PKQE | QXD | . КЕНҮРР: | SASLK | SLFGN | DPLSQ | |
| . WINIED MAD | | | S R | | | Q | P | | i. | | s | |
| ISOLATE-E | F | PTAPPAE | NW.GP | GEE | · • • • • | (| QXO | KEHPPPS | vslk | SLFGNI | PLSQ | • |
| CONSENSUS-A | | EPLAPDAE. | ?f?g | maeair | 62 | | | 2122- | | | | • |
| CONSENSUS-B | ????? | e | · · · · · · S - · I | #90010 ft- | tneiz | pkqe | egika: | rkerrpp | 1,811 | CSIFGN | mp1sq | . 485 |
| Consensus-C | | | | P . ~ - F - | na | | . n 22 | 2 2 | • | | | |
| | | | · · · · · · S | F | De | ~ | 22 | 3 | _ | | x | 479 |
| CONSENSUS-F | | | | ~~~~ | DC | | | | _ | | | 495 |
| 40110 PHO 00 - G | | : | - 7 . 7' | 77? | 20 | | D22 | | | | | 482 |
| | | | S l | 7M- | D_ | | 22 | | | | | 440 |
| CO110701207-0 | | | | - 2VX | 20 | E-17 2 | ~ | 2 | | _ | 00 | 436 |
| CONSENSUS-CPZ | • • • • • • • | ·I | Y.? | Q?K | ? | 2-77 | ??? | | | T | -UŞ | 444 |
| | | | | | | | | 5 | | | | 333 |
| CONSENSUS A-CPZ | z From I | os alamos | HIV SEQUE | NCE DA | TABAS | E | | | | | | |

CONSENSUS A-CPZ FROM LOS ALAMOS HIV SEQUENCE DATABASE ISOLATE-E SEQ FROM ISOLATE 93TH253 THAILAND

Underlined AA are not present in all overlapping segments

FIGURE 3 (Cont)

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| DESIGNED SE | Q FFRE.NLAFQOGKAREFSSEQTGANSSASRKLGDGGGAERQ P B P R PT D | |
|---|--|--|
| ISOLATE-E | PFRE.NLAFQQGKARBFSSEQTGANSSASRKLGDGGGAERQ | |
| CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-O CONSENSUS-U CONSENSUS-CP | FFRE.NLAFQQGEAR?F. SSE.QT??NS?TSR?LWDGG?D??.L????G?E?.Q dp-k-e-?????????????Ra-p-r-B-qVw-r-nnS-S???-BA-adr t | 3 4 4 3: 4: 1: |
| | protease // <- gag cds end | , |
| DESIGNED SEQ MUTATED AAS | GTSSSFSFPQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEDINLPGKWKPKMIGGIGGPIKVRQYD LN V I EM R | |
| ISOLATE-E | GISSSFSFPQITLWQRPLVTIKIGGQLKBALLDTGADDTVLEDINLPGKWKPXMIGGIGGFIKVRQYD | |
| CONSENSUS-A COMSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-O COMSENSUS-U CONSENSUS-U | G???SF?FPQITLWQRPLVTV?I?GQLIEALLDTGADDTVLEDINLPGKNKPK?IGGIGGFIKVRQYDtVsik-gK | 96 116 115 94 115 55 |
| | protease \/ p66, p51 QILIBICGKKAIGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIDTVPVKLKPGMDGPRVKQWPLTEEKI I <u>H</u> L L R E | |
| ISOLATE-B | QILIEICGKKAIGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIDTVPVKLKPGMDGPKVKQWPLTEEKI | - |
| Consensus-à Consensus-b Isolate-C Consensus-d Consensus-o Consensus-U Consensus-CP2 | QILIBICGKK?IGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIETVPVKLKP?MDGPKVKQWPLTEEKI | 164 186 184 159 185 106 |
| | M41L D67N K70R KALTBICKEMEEEGKISKIGPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRIQDFWEVQLGIPHPAGLK | |
| OESIGNED SEQ OUTATED AAS | ATK R I | |
| ISOLATE-B | Q Kaltbickembébegkiskigpenpyntpvpaikkkostknrklvoprelnkrtoopwevqlgiphpaglk | |
| Consensus-A Consensus-B | KALT?IC?EMEKEGKISKIGPENPYNTPVFAIKKKDSTKWRKLVDYRELNKRTQDFWEVQLGIPH?AGLKVET | 231 256 |
| CONSENSUS-D CONSENSUS-O | A-BQR | 254 227 255 164 |
| | KKKSVTVLDVGDAYFSVPLDESFRKYTAFTIPSINNETPGIRYQYNVLPQG#KGSPAIFQSSMTKILEPF KD T P PQ . | |
| SOLATE-E | g KKKSVTVLDVGDAYFSVPLDESFRKYTAFTIPSINNETPGIRYQYNVLPQGWKGSPAIFQSSMTKILEPF | |
| Onsensus-a Onsensus-b Solate-c | KKKSVTVLDVGDAYFSVPLD??FRKYTAFTIPS?NNETPG?RYQYNVLPQGWKGSP?IPQ?SMTKILEPF | 295 326 |
| Onsensus-d Onsensus-d Onsensus-u | O?QBDIIAS | 324 295 325 225 |
| | | |

polymerase motif

FIGURE 4

| | | | | DE DE DOMINOS : | • |
|--------------------------------|---------------------------------------|---|---|-------------------|------------|
| DESIGNED SEQ MUTATED AAS | QPIELPEKDSWTVNDIQKLVGKLNWAS V E | P R | a e t | A | |
| isolate-e | Q QPIELPEKDSWTVNDIQKLVGKLNWAS | QIYAGIKVKQLCKLI | rgtkaltdivplteea | BLELEENREI | |
| CONSENSUS-A | QP??LPEKDSWTVNDIQKLVGKLNWA | SQIYAGIK?KQLC?L | LRGAKALTDIV?LTEE | aelelaenrei | 4: |
| CONSENSUS - B | Iv | XX- | tEvip | | 46 |
| ISOLATE-C | IQB | pvkk | TEViP | | 46 |
| CONSENSUS - D CONSENSUS - O | -:10:: | ORV?EK- | IT-SEV-P-S? | B? | 41 |
| CONCENSUS-II | 10D-E | PVK- | PA | | 46 |
| CONSENSUS-CPZ | -?I??? | P | I?-??-?-?- | ???-?? | 32 |
| DESIGNED SEQ | . LREPVHGVYYDPSKDLVAEVQKQGQD | | TGKYSRKRSAHTNDVR | | |
| HUTATED AAS | K II G | , | | . AA <u>V</u> | |
| :ISOLATE-B | .LRIPVHGVYYDPSKOLVAEVQKQGQD(| | | | W. |
| CONSENSUS-A | . LK?PVHGVYYDP?KDLVAE?QKQGQL | XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX | CTGKYA?KRSAHTNOVK | OLIEANOKASSE | 484 |
| CONSENSUS-B | e | | PT | ATA1 | 53: |
| | E | | Rm-G | a-aIsT- | 531 |
| CONSENSUS-D | Q-DWV?I?-?? | ??EH | ?ROKASIR | A?SQ- | 479 |
| CONSENSUS-U | BG | QY | RIK | AIAQ- | 532 |
| CONSENSUS-CPZ | ???-???-???-?!?? | ?-????-? | ?R???????R | A??I | 367 |
| | | • | p: | 51 | |
| DESIGNED SEQ | IVIWGKTPKPRLPIQRETWETWWMEYW | QATWIPEWEPVNTPP | LVKLWYQLEKDPIVGA | ZTFYVDGAASR | |
| MUTATED AAS | K . K A TD | | EAV | Ŋ | |
| | IVIWGKTPKPRLPIQRETWETWWMEYW | | | • | |
| Consensus-A | SIVINGK?PKFRLPIQ?ETWE?WWMEY | nqatwipewbpvntp | PLAKEMAGERKOBI SCA | ETPYVDGAANR | 550 |
| CONSENSUS-B | tkKt | | | | 602 |
| ISOLATE-C - | TKT? | | EI | | 600 |
| Consensus-d Consensus-o | ?-?L?VTRTA? | s | I??E | ? | 541 |
| ONSENSIS-II | TKAT | | TEV | | 602 |
| CONSENSUS-CPZ | ????A?? | | ???-??? P ?? | ?-? | 416 |
| ESTENED SEO E | tklgkagyvtdrgrqkvisltettnqkt | relhathlalqdsgsi | EVNIVIDSQYALGIIQA | OPDRSESEVV | |
| STATED AAS | IV D | O O F | L | K L | |
| | tklgkagyvtdrgrqkvisltettnqkt | | | • | |
| ONSENSUS-A | etk?gkagyvtdrgrqkvvsltettnqk | TELHAIHLALODSGS | Bunividsqyalgiiq | AOPDRSESE?V (| 618 |
| ONSENSUS-B | 1d | dJ | | k1- 6 | 672 |
| SOLATE-C - | -III | QQ | | KI- | |
| ONSENSUS-D | L | QNL | 2 | KD- 6 | 670 602 |
| | ?LEQ-K-?IIK-? | OKB | ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,, | ,KT- 6 | 572 |
| onsensus-u Onsensus-CPZ | ???Q | A?-?L???? | ????- | ????L4 | 159 |
| | | unio utoothicut et | TO THE NOTE HE DANCED | уртмастітат. | |
| esigned seq so Utated aas n | DIIEELIKKEKVYLSWVPAHKGIGGNEQ K R A | SA SA | D K | NE | |
| SOLATE-E S | Q DiieelikkœkvylswvpahkgiggneQ | VDKLVISGIRKVLFL | DG I NKAQEEHERYHSM | irtmasdfnl | |
| ONSENSUS-A 1 | QIIEKLI?K?KVYLSWVPAHKGIGGNE | OVDKLVS?GIRKVLF | LDGIDKAQE?HE?YH? | IW?AMASDFNL 6 | 81 |
| ONCENCIE-B | aK-Ea | aa- | eKs- | -r 7 | 142 |
| - 3-3T4.102 | 0S-ER | S | | -RNEI | |
| ONCENCIE-D | OK-EA | | BKN- | R 7 | 140 |
| ONCENCIE-O | R-TK-E?T | (IKDR | -EQDKS- | ·L?-G- 6 | 69 |
| ONO PROPERTY IN | 00-D | | EKS- | -R 7 | 142 |
| ONSENŜUS-CPZ | ????K?E?I | | -???S- | ??-??? 5 | |
| ESIGNED SEQ PI | PIVAKEIVANCDKCOLKGEAMHGOVDCSI | | | PAETGOETA | |
| UTATED AAS | PS IN | I | | | |
| | С | | | | |

FIGURE 4 (Cont)

| | · | |
|---------------|--|------|
| ISOLATÉ-C | LRB- | |
| CONSENSUS-D | 1 | 880 |
| CONSENSUS-0 | LASQD- | 798 |
| CONSENSUS-U | YB- | 882 |
| CONSENSUS-CP | | 631 |
| WH3BH305-CL | | |
| DESTGNED SEO | AEHLKTAVOMAVFIHNFKRKGGIGGYSAGERIIDIIATDIQTKELQKQITKIQNFRVYYRDSRDPIWKGP | |
| MUTATED AAS | R V S N L L | |
| HOINIED ME | - | |
| ISOLATE-E | AEHLKTAVQMAVFIHNFKRKGGIGGYSAGERIIDIIATDIQTKELQKQITKIQNFRVYYRDSRDPIWKGP | |
| | AEHLKTAVQMAVPIHNPKRKGGIGGYSAGERIIDIIA?DIQTKELQKQI?KIQNFRVYYRDSRDPIWKGP | 880 |
| CONSENSUS-A | AEHLKTAVQMAVFIHNFKRGGIGGISAGBRIIDIIA:DIQIALIQAQI: KIQATAV IIIDDIGI | 952 |
| CONSENSUS-B | | 232 |
| ISOLATE-C | iii | 950 |
| CONSENSUS-D | | 865 |
| CONSENSUS-O | | 952 |
| CONSENSUS-U | | 687 |
| CONSENSUS-CP2 | | |
| | vif cds -> | |
| DESTGNED SEO | AKILINKGEGAVVI QDNSDI KVVPRRKAKI IRDYGKQMAGDDCVAGRQDED | • |
| MUTATED AAS | A S | |
| MUTATED AAS | | • |
| ISOLATE-E | AKLLWKGEGAVVIODNSDIKVVPRRKAKIIRDYGKQMAGDDCVAGRQDED | |
| 130DM1P-P | · | |
| CONSENSUS-A | AKLLWKGEGAVVIQDNSDIKVVPRRKAKIIRDYGKQMAGDDC?AGRQDED | 929 |
| CONSENSUS-B | | 1002 |
| ISOLATE-C | | |
| CONSENSUS-D | | 1000 |
| CONSENSUS-O | -OT-SM-NT-SESMEQPGEIP | 925 |
| CONSENSUS-U | V-GKHGTAW | 100B |
| CONSENSUS-CPZ | -?OGEL | 742 |
| | • | |

CONSENSUS A-CPZ FROM LOS ALAMOS HIV SEQUENCE DATABASE ISOLATE-C FROM GENBANK U46016 HIV-1 SUBTYPE C (ETHIOPIA) ISOLATE-E FROM GENBANK U51189 HIV-1 SUBTYPE E ISOLATE 93TH253 (THAILAND)

<- pol cds

| DESIGNED SEC | MENTON O | VIMITUMO | VIDRMR TR | TWNSLVI | KHHMYIS | KKAKGN | PYRHH | YESOH | PKVSSEV | HIPLGE. | . ARLVI | • |
|---------------|------------|------------|-------------|----------|----------------------|---------|---------------------------------------|--------------|----------|----------|---------|-------|
| MUTATED AAS | , MEMANA.Q | L | K | K | H | N | J | FD R | | D | 1 | |
| ISOLATE-E | MENRW.Q | DHVINV. | /DRMRIR | Twnslv | CHMYIS | KKAKQW | FYRHH! | YESQHI | Kassra | HIPLGE. | .ARLVI | |
| CONSENSUS-A | MENRN. | OWVINV. | VDRMrI | RTWNSLV | KHHMYV | SKKARG | NFYRH | if Esri | lpkvsSE | VHI PLGd | ARLVV | 66 |
| CONSENSUS-B | | VLIVWQV | | k | | -0 | | ·Yt- | -rı | | 1 | 66 |
| ISOLATE-C | MENRW Q | APIAMOA | DRMKIK | TMN2TAY | HHMH12 | | , , , , , , , , , , , , , , , , , , , | -a-by | I | B | | 65 |
| CONSENSUS-D | | L- | 2 - 01/17/1 | (h | -V-Y-2 | 2-22N. | .2 | YN | -?? | -YV?? | ?? | 54 |
| CONSENSUS-OP | Z -????.? | ??? | | ?-? | -?-I??? | -????- | ? | Y???? | ???- | ????? | 3.5K-5- | 34 |
| DESIGNED SEQ | RTYNGLOT | rcekowa. | GRGVSTI | WROKRY | STOVDPI | LADOLI | HLOYP | DCFSD | STIRRA | ILGQIVRF | URCEYP | |
| MUTATED AAS | | R H | | LS | | н | Ħ | A | A | HR S | Q | |
| HOINIDD INC | | | | K | | _ | ¥ | | | | | |
| -007 NWR F | RTYNGLQI | MIDWINE . | CUCUSTE | NDOKRY: | STOTEP | LADOLI | HLOYF | DCPSD | STIRRA | ILGQVVRR | RCEYP | |
| ISOLATE-E | | | | | | | | | | | | |
| CONSENSUS-A | RTYWGLH | TGExDWH | LGhGVSI | ENTOKR | YSTQ V DP | DLADqL | IHLhY | FACES | asairki | AILGeiVR | PRCBYO | 136 |
| CONSENSUS-B | - | | • | k | | | V- | (| en· | n~-s | | 136 |
| ISOLATE-C | PHYDDIAT | LIUMI GOST | CUCVSTE | WRT.RSY1 | NTOVDPG | LADHLI | нмнуг | DCLAE | SWIKKY. | TRASE | KCDIO | |
| CONSENSUS-D | 3 - | | 0 | KD | | G | MY - · |] | 87 | ·b5 | ? | 132 |
| CONSENSUS-0 | TM | P3E- | | ?Y-?- | -KI | etrm | | -TT | ?? | QR-L | TK? | 118 |
| CONSENSUS-CP | Z T??-?-? | | | ??G?- | ? | ?T?? | ??- | -?? | ??-?-?- | ????? | ??-?-K | 76 |
| | | | | | νp | r cds · | -> | | | | | |
| DESIGNED SEQ | SCHNICKGS | LOYLAL . | (ALI | TPKKIRE | PLPSVK | KLTEDRI | NNKPQ! | KI KGHI | RENHTM | GH | | |
| MUTATED AAS | A | | | K K | | R | B | T R | G | | | |
| | | | | | | | | | | | | |
| isolate-e | SCHNIKVGS | LQYLAL.I | CALT | TPKRIRP | PLPSVK | KLTEDRI | NNICPQ: | CIKGHI | (EN PIMA | GHŞ | | |
| CONSENSUS-A | AGHNKVG | SLQYLAL. | kal | VaPtkaK | PPLPSvl | KLtEDF | WneP(| KTRGE | IRG\$R?¤ | NgH\$ | | . 191 |
| CONCENSING-B | | | a | it-k-i- | | · | K | · K | ht- | | | 191 |
| ISOLATE-C | ACUMICUCS | LUALTE A | ד זמי. | KDKKAKP | PI.PSVSI | C.VEDK) | NKPOJ | (TRGKH | CNHILL | GH | • | |
| CONSENSUS-D | 2 | | t 1 | K-T- | F | } | K | k | ?HT- | | | 186 |
| CONSENSUS-O | 2607 | P7 | 7-V | K????- | |)? | K?? | ?I-D0 | L?-?S- | | | 161 |
| Consensus-CP2 | ??0 | ???? | -?-??? | ?????R | ????? | ? | K?? | R???- | ?EN?TR | | | 107 |

| | | | | | | | • . | · • • | |
|---------------|--------|---------------|-------------|---------------|--------------------------------|---------|-----------------|-----------|----|
| : | | | <- | vif cds | | | • | LR domain | |
| • | /<- | | oligomeri | zation | ->/ | , | | /<- | , |
| DESIGNED SEC | MEO. | ND PROGRAPE | DVMPWAT.ET. | r.PRT.KOPAUDI | UPDD DWI UNI C | OVIVET | Kantusaurai | (TPTLOO | • |
| MUTATED AAs | , MEG | SS | T | Н | Ğ | H | E | I | |
| MOINIED AND | | 33 | • | N. | | ** | • | • | |
| ISOLATE-E | MEQ | AP EDQGPQRE | PYNEWALELI | LEELKQEAVRI | ifpr pwl hin l g | QYIYETY | GDTWSGVEAL | IRTLQQL | |
| CONSENSUS-A | ME?. | .AP.EDOGPORE | P??E??LEL | LEELKHE?VR | HFPR?WLHGL | GOHIY?T | YGDTWEGV?A | JIRILOOL | 58 |
| CONSENSUS-B | | ?? | | | | | | | 69 |
| ISOLATE-C | | AP EDOSSORER | | | | | | | ٠. |
| CONSENSUS -D | | | | | | | | | 64 |
| CONSENSUS-O | 0. | na | -fN-Wt | ?-A | pa | vB- | m- | | 66 |
| CONSENSUS-U | | A | | | | | | | 67 |
| CONSENSUS-CP2 | | | | | | | | | 33 |
| | | | | | | | | | |
| | 0 | LR domain ->. | / tat cd | s -> | | | | ē | |
| DESIGNED SEQ | MFIH : | PRIGCOHSRIGI | L RQRRA | RNGASRS | | • | | | |
| MUTATED AAS | L V | R | r G | S | | | | | |
| ISOLATE-E | MPTU I | PRIGCOHSRIGII | . POPPA | RNGASRS | | | | | |
| | | | | | | | | | |
| CONSENSUS-A | LF?H. | FRICCOHSRIGI | I?GRRG | .RNGA?RSS | | | | | 84 |
| ONSENSUS-B | | ?r | | | | | _ | | 93 |
| | | RIGCOHSRIGIE | | | | | • | | |
| ONSENSUS-D | | | | | | | | | 93 |
| ONSENSUS-O | | y | | | | | | | 94 |
| ONSENSUS-U | | | | | | | | | 96 |
| ONSENSUS-CPZ | ??I | ????-?? | LPQR | .SSN | | | | | 54 |
| | | | | | | | | | |

| | intramolecular 3'sj 3'sj disulfide bonding \/ \/ | : |
|---------------|---|-----|
| : | rev cds>/<- nls ->/ | |
| DESIGNED SEO | MDPVDPNLBPWNHPGSQPTTACSKCYCKKCCFHCQLCFLKKGLGISHGRKKR KQRRGAPQSRKDHQYP | |
| MUTATED AAS | KK KT YVT Y RRS <u>e</u> | |
| 1 | . и <u>Q</u> | |
| ISOLATE-E | MELVDPNLEPWNHPGSQPTTACSKCYCKKCCWHCQLCFLKKGLGISHGRKKR KHRRGTPQSRKDHQYP | |
| CONSENSUS-A | M?PVDPnLEPWnHPGSqPtTaCskCYCK?CCwHCqlCPLnKGLGISYGrKKRr?RRgtPQs?kDhQnp | 64 |
| CONSENSUS-B | -ekktnkfvttQradSqtvs | 68 |
| CONSENSUS-C | ?Ktk-sYlVqtgsa-?-SE | 65 |
| CONSENSUS-D | -d | 66 |
| CONSENSUS-F | -ELDP-TRFWTTKQ-HRSQIDL | 68 |
| CONSENSUS-O | -DE?PH?-Q?P-NNRYYV???????AAAP-?KD- | 55 |
| CONSENSUS-U | -DKKTKYPV | 68 |
| CONSENSUS-CP2 | -D-?-?????-??-?-NNY??TK?-???T????S?NN-D? | 45 |
| е | oton _. \/ exon | |
| DESIGNED SEQ | I PEQPLPQTRGGNPTDPKESKKEVASKTETDPCD | |
| MUTATED AAs | S SPD GE KEAP | |
| isolatė-e | I PEQPLPI I RGGNPTDPKESKKEVASKAETDPCD | |
| CONSENSUS-A | ipKQplPqtqg??ptgpkESkKkVeSKteTDrf?\$ | 95 |
| CONSENSUS-B | Ls?s-pr-DrEP?d? | 99 |
| CONSENSUS-C | -sr-dEp-D- | 98 |
| CONSENSUS-D | SS-pR-d? | 99` |
| CONSENSUS-F | VIS-AR-N | 96 |
| CONSENSUS-O | V-?-5???-?RK.Q?RQE-QE??K??GP?G?P????SC??CTR?S?Q\$ | 83 |
| CONSENSUS-U | SHRV.SEBD- | 101 |
| | nn | 52 |

| | | | • | | bindi | affinity ing site | <i>r</i> | | | | |
|-----------------|------------------------|-----------|-------------|----------|----------|----------------------|---------------|-------|-------|-----|-----|
| | \/ 3 ' sj | | exon \/ e | | /<- | nls | ·> <i>j</i> : | | | • | |
| | (/ 3 8) | | exon () (| exon | /<- | | `>/ | | | | |
| DESIGNED SEC | MAGREGETDE ELI | RAVRIIN | ILYQSNPYI | PSSEG TI | OTRKNER | RRWRAROR | OIRAI | SERIL | STCLG | irs | |
| MUTATED AAS | D | KI K | | S | AR | В | . HS | W | NĖ | P | |
| | N | | | | | | | | | | |
| ISOLATE-E | MAGRSGSTDE ELL | RAVRIIN | LYQSNPYF | PSSEGGTE | QTRKNRR | RRWRARQR | QIRAIS | ERIL | STCLG | RS | |
| CONSENSUS-A | MAGRSG?sDE.eL | L.KAIRIIN | (i LYQSNPy | PkPkG.S | ROARKNR | RRRWRARQ | RQIDS1 | SeRII | StCL | GRP | 66 |
| CONSENSUS-B | d | tV-l | fp | -s-eT | R | e | r-i | w | y- | s | 67 |
| ISOLATE-C | MAGRSGDSDE ELL | KAVRIIKI | LYOSNPYP | TPEG TR | QARRNRR | RRWRARQR | QIHTLS | ERILS | NPLG | RP | |
| CONSENSUS-P | N-?T | | | | | | | | | | 61 |
| CONSENSUS-O | BQ? | -?QQ | | -?-? | -N | R1 | A-V-?- | A?-?- | A-VVI | iG? | 56 |
| CONSENSUS - U | DA | RVV | | -P-BT | -T | | RAI | P- | | s | 67 |
| CONSENSUS - CP2 | Z?E-?????? | ·??-VK | ? | -?-?? | ·?R-?· | ??? | ?-???? | ??-V- | ?-??- | | 41 |
| | • | | | | • | | | | | | |
| | Leu-ri | | | | • | • | | | | | |
| | effector | | • | | | | | | | | |
| | /<- | ->/ | | | | | | | | | |
| DESIGNED SEQ | AEPVPLQLPPLERL | LDCSEDCG | TSGTQQSQC | FTETGVG | PQISGES | SVILGPGT | KN | | | | |
| MUTATED . AAs | N | r SD | | <u>N</u> | <u>L</u> | AV S | | | | | |
| | | | | S | | | | | | | |
| isolate-e | TEPVPLQLPPLERLH | LDCSEDCG | rsgroosog | TETGVGR | PQISGES | SVILGPGT | KN | | | | |
| CONSENSUS-A | AEPVPLQLPPlerL | hLDCsEdco | TSgTQq?q | q?etGVG | rpQvsVE | ssavLGSG | Tkn | | | | 120 |
| CONSENSUS-B | | | | | | | | | | | 115 |
| ISOLATE-C | AEPVPLQLPPLERLN | LDCSEDSD1 | CSCTQQSQG | TTEGVGN | P PREMA | TURE TRU | NCATED |) | | | |
| CONSENSUS-F | E? | ?IN?2-E | Q-A?E | | ST-G- | -н | E\$ | | | | 105 |
| CONSENSUS-0 | Q?NN?VDQ- | ?IRDP-?D? | L????TVD | PRAEDN\$ | CL-NLCS | NT????? | ???N\$ | | | | 95 |
| CONSENSUS-U | I | CG | P- | -T | S-PI-G | TI | E\$ | | | | 123 |
| SOMEONICH CD7 | DY-CD-9-9-DY-6 | 2-0-11 mm | DU - CAPPEC | 3DO 877 | | TWOT W 1 | | | - | | |

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| | | • | | | • | | | pho: | cds - | > phos | |
|-----------------|-----------|-------------|------------------|---------------|------------|---------|------------|-----------|---------|-------------|---|
| DESIGNED SEQ | MTPL | EIIAIVAPI | /ALIIAIVV | WTIAYI | EYRKL | LRQR | RIDRL | IKRTRERA | EDSG | NES | |
| MUTATED AAs | | L | L | VP | . <u>к</u> | K | K | EI | | | |
| CONSENSUS-A | mtPL??? | eIcAIvGLi | VALILAIV | vwrivgi | .eyKkl | lkqr | Kidrl | ?ikRIrER# | A. EDSg | NES 57 | , |
| CONSENSUS-B | -qs- | q-?a-v | a-i | £- | ?r-i | -R | ? | d | | 56 | , |
| ISOLATE-C | MVDLLAK | VDÝRIVIVAFI | VALIIAIV | MTIAYI | EYRKI | LRQR | RIDRL | IKRTRERA | EDSG | nes | |
| CONSENSUS - D | -0 | v-1A-v | i | £- | crr- | kr | w- | d | ? | 57 | |
| CONSENSUS-F | -S?? | LAIS?TA | I | ?Y- | R | -R | N | .YE?? | | 51 | |
| CONSENSUS-0 | -H?? | ?LL-?I??S | AL??INV?? | -?F? | LR?Y | -?-??QI | DR?E?R-LER | .LR?-IR | .DD | Y 42 | |
| CONSENSUS-U | -0 | | | | | | | | | | |
| CONSENSUS - CPZ | _ | | | | | | ??????-? | | | | |
| DESIGNED SEO | EGDTBE LS | STM VDM | GNYDLGVDN | INL | | | | | | | |
| MUTATED AAs | R | AL | | | | | | | | | |
| CONSENSUS-A | ?GDT?E.L | ?kLVEM | .Gnydlgvd | nNL\$ | | | | | | 78 | ļ |
| CONSENSUS - B | eqe | sa-???? | ?-H?apwdv | dD | | | | | | 79 | ı |
| SOLATE-C . | DGDTÉE LS | TM VDM (| INLRLLDVN | \mathbf{DL} | | | | | | | |
| ONSENSUS - D | ErE | sa | -HhAPwd? | Dcm- | | | | | | 80 | |
| CONSENSUS-F | BAE | A?G | -PFIP-DI | ? | | | | | | 73 | |
| ONSENSUS-O | N?EE-QEV | M???SI | I-F?NPM.F | B?? | | | | | | 59 | |
| ONSENSUS-U | | STM | | | | | | | | 81 | |
| ONCENETIC CD7 | -28822 | | PAND? ? | 222DB | | | | | | 23 | |

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<- vpU cds signal peptide / gpl20

| • | | · | |
|------------------|-------------------------------|--|-----|
| DESIGNED SEQ | MRVKETOMNIPNI WK | W GTLILGLVIIC SA SD NLWVTVYYGVPVWRDADTTLFCAS | |
| MUTATED AAS | R | M M M E ET . | |
| | | and the state of t | |
| consensus-a | | ????W.gtmilg??iIc.na??e.?lWVtVyYGVPVWkdaeTTLfcAS | 4 |
| CONSENSUS-B | | ?????e-t | 5 |
| CONSENSUS-C | | e-k | 5 |
| CONSENSUS - D | | ?????E-t | 5 |
| CONSENSUS - E | Ket-m-wpnk | rd | 5 |
| CONSENSUS - P | -?-R-M-R-W-HGK | e-T | 5 |
| CONSENSUS-G | -?-kr-W-Hk. | ELLVssn.nED | 54 |
| CONSENSUS-O | -t-tMKaM?KrNr.Kl. | ?lylamALi-PLS??Q-YAsE?Pv | 5: |
| CONSENSUS-U | | ??????-?-? | 36 |
| CONSENSUS-CPZ | | ???????-????.?T?????-?P?? | 19 |
| 0,000,000 | | | *- |
| | | • | |
| | · | m with any 120, and 10 verapose of management and the continuous | |
| | | VPTDPNPQBIHLB NVTENPMMWWMWEQMQEDVISLWD QSLKPCVKLT VV D D H I | |
| MUTATED AAS | YD | VV D D R I | |
| | Ja I. a A. Managara a mar. of | | |
| Consensus-A | • | TVPTDPnPqBi?le.NVTB?FnmwkNnMVeQmheDiiSLWD.qSLkPCvkLt | 113 |
| CONSENSUS-B | | | 119 |
| CONSENSUS - C | | | 119 |
| CONSENSUS-D | | | 117 |
| | | | 121 |
| | | T, | 120 |
| | | EE | 120 |
| | | ?-?-!p-?dIYdqM- | 114 |
| CONSENSUS-U | ?-?? | ????? | 91 |
| CONSENSUS-CPZ | ?-???\$??? | ??-??V????????-????-??? | 56 |
| | | | |
| | * * | | |
| | | | |
| DESIGNED SEQ PI | LCVTLNCTNANLINVN · | HYPERVARIABLE REGIONS 1/2 | |
| MUTATED AAS | | • | |
| | | | |
| CONSENSUS-A E | LCVTL?C . ???????????? | n?t?????????n?t???????n????????????? | 126 |
| CONSENSUS-B - | ntd | ?-???????- | 133 |
| | | ??? | 132 |
| | | ????????????? | 131 |
| | | -l????? | 150 |
| | | -at-?-?-q?tLkB | 139 |
| | | -Vt?-?NcT?ennNstv??? | 143 |
| | | | 129 |
| | | | 105 |
| | | | |
| CONSENSUS-CPZ - | r- | · · · · · · · · · · · · · · · · · · · | 60 |
| | ^_^ ^ | • | |
| | - | | |
| | | to | |
| DESIGNED SEQ | HYPERVARIABI | LE REGIONS 1/2 | |
| MUTATED AAS | | | |
| | | • | |
| CONSENSUS-A ? | ?eikNCsfNmTte | elrdkkqkvysLfYrlDvVqi???????n???????n????????? | 160 |
| CONSENSUS-B e3 | ??q-?????is | sive-akp-d?????? | 169 |
| | | | 166 |
| | | | 165 |
| | | | 185 |
| * | | | |
| | | | 177 |
| | | | 182 |
| | | | 164 |
| | | | 137 |
| CONSENSUS-CPZ -? | ?-????-???-? | ???????????-????T | 73 |
| | • | • | |
| | *^^^ | * | |
| 4. | | | |
| DESTGNED GEA VOT | TNONTSVTKOLOBUSEND | PIPIHYCAPAGYAILKCNDKNFNGTGPCKNVSSVQCTHG IKPVVSTQL | |
| - | | F NK T T R | |
| eaa detatum | S AT ITE | r nk 11 k | |
| | | r · | |

FIGURE 10

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| CONSENSUS-I | nrrnk | 234 |
|---|--|--|
| | i D | 254 |
| CONSENSUS-E | | |
| CONSENSUS-E | ?TWGINK | 245 |
| CONSENSUS-G | v-T-Kn-drnrn | 251 |
| CONSENSUS-C | | 228 |
| | | - 205 |
| CONSENSUS-U | | 120 |
| CONSENSUS-C | bz - //// | 120 |
| | | |
| | <- V3 neutralization loop | _ |
| | AAA . AAA . AAA | |
| | | |
| | O LLNGSLAEE EIIIRSENLTNNAKTIIVHLNESVEINCTRP NNNTR K HYPERVARIABLE REGIO | N 3/4/5 |
| | | 3/4/3 |
| mutated aas | <u>vv</u> fdv gkv s t | |
| | | |
| CONSENSUS-A | <pre>LLnGSLAe???v?irSenitnNaktiiVql??pV?InCtRP.nnntr.ks???vri???gpGq??afya.</pre> | 279 |
| CONSENSUS-B | e.e.e-vf-dnes-e?ihrt. | 296 |
| CONSENSUS-C | eiilvh-n-s-e-viit | 291 |
| | g. BiI1?nes?y?qrtp?l-t? | 288 |
| CONSENSUS-D | e.elih-NKs-estitvr. | 312 |
| Consensus-E | e.diiqsdh-Nes-q!?!? | |
| Consensus-P | e.dl1qsqnes-q | 302 |
| CONSENSUS-G | e.eI?-dvnksie-? | 305 |
| CONSENSUS-H | ?D-T-NK | 39 |
| CONSENSUS-0 | IT-Skg.kIr-Mgk?dsg-NT-N-?i-mt-eg-?-v.Qei?mW-S. | 279 |
| CONSENSUS-U | B.E-i?dnet-k??? | 261 |
| CONSENSUS-CI | | . 142 |
| CONSENSUS-CE | 2 | |
| | CTA | |
| V3 ne | utralization loop -> CD4 | |
| | | |
| | | |
| DESIGNED SEC | HYPERVARIABLE REGION 3/4/5 | |
| MUTATED AAS | • | |
| ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,, | | |
| CONSENSUS-A | tgdiiG.dirqAhCmvsr?eWn?tlq?Va?qLr??f???nkt??iiP?n.ssGGD | 320 |
| CONSENSUS-B | ?-???iaknkqiv-ke??qv-nq? | 342 |
| • | and the same of th | |
| | | |
| CONSENSUS-C | | 334 |
| CONSENSUS-C CONSENSUS-D | -?r?????-?i-?a?kgk-qd?.lltkp | 331 |
| | -?r?????-?i-?a?kqk-gd?.lltkp k-y-EINgTke?-kqtek-keHnq ^p ?p | 331 360 |
| CONSENSUS-D | -?r?????-?i-?a?kqk-gd?.lltkp k-y-EINgTke?-kqtek-keHnq ^p ?p ?kqtge?a?-ksh?k-ns | 331 |
| Consensus-e Consensus-e Consensus-f | -?r?????-?i-?a?kqk-gd?.lltkp k-y-EINgTke?-kqtek-keHn | 331 360 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-G | -?r?????-?i-?a?kqk-gd?.lltkp k-y-EINgTke?-kqtek-keHn | 331 360 344 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-G CONSENSUS-H | -?r?????-?i-?a?kqk-gd?.lltkp k-y-EINgTke?-kqtek-keHn | 331 360 344 344 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-G CONSENSUS-H CONSENSUS-O | -?r???? . ? - ? i - ?a? - k q k - gd? . l l t kp qP?p | 331 360 344 344 65 321 |
| CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - G CONSENSUS - H CONSENSUS - O | -?r???? .?-?i-?a?kqk-gd?.llkpk-y-EINgTke?-kqtek-keHn | 331 360 344 344 65 321 306 |
| CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - G CONSENSUS - H CONSENSUS - O | -?r???? . ? - ? i - ?a? - k q k - gd? . l l t kp qP?p | 331 360 344 344 65 321 |
| CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - G CONSENSUS - H CONSENSUS - O | -?r???? .?-?i-?a?kqk-gd?.lltkpk-y-EINgTke?-kqtek-keHnqP?p? | 331 360 344 344 65 321 306 |
| CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - G CONSENSUS - H CONSENSUS - O | -?r???? .?-?i-?a?kqk-gd?.llkpk-y-EINgTke?-kqtek-keHn | 331 360 344 344 65 321 306 |
| CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - G CONSENSUS - H CONSENSUS - O | -?r???? .?-?i-?a?kqk-gd?.llkpk-y-EINgTke?-kqtek-keHnqP?p?kgtqe?a?-kshk-nsa?-?em-n?-?i?-? | 331 360 344 344 65 321 306 |
| CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - G CONSENSUS - H CONSENSUS - O CONSENSUS - U CONSENSUS - CP | -?r???? .?-?i-?a?kqk-gd?.lltkpk-y-EINgTke?-kqtek-keHnqP?p? | 331 360 344 344 65 321 306 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-G CONSENSUS-H CONSENSUS-U CONSENSUS-U CONSENSUS-CP: | -?r???? .?-?i-?a?kqk-gd?.llkpk-y-EINgTke?-kqtek-keHnqP?p?kgtqe?a?-kshk-nsa?-?em-n?-?i?-? | 331 360 344 344 65 321 306 |
| CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - G CONSENSUS - H CONSENSUS - O CONSENSUS - U CONSENSUS - CP | -?r???? .?-?i-?a?kqk-gd?.llkpk-y-EINgTke?-kqtek-keHnqP?p?kgtqe?a?-kshk-nsa?-?em-n?-?i?-? | 331 360 344 344 65 321 306 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-H CONSENSUS-U CONSENSUS-U CONSENSUS-U CONSENSUS-CP: | -?r???? .?-?i-?a?kqk-gd?.lltp | 331 360 344 344 65 321 306 157 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-CP: DESIGNED SEO MUTATED AAS CONSENSUS-A | -?r???? .?-?i-?a?-kqk-gd?.lltkpk-y-EINgTke?-kqtek-keHnqP?pkgtqe?a?-ksh?k-ns?-?em-n?-??? | 331 360 344 344 65 321 306 157 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-CPS DESIGNED SEQ MUTATED AAS CONSENSUS-A CONSENSUS-B | -?r???? .?-?i-?a?-kqk-gd?.lltkpk-y-EINgTke?-kqtek-ke. HnqP?pkgtqe?a?-ks. hk-ns?-em-n?-?-i? .?t-nsa ?-??-!??-?-?-?-? | 331 360 344 344 65 321 306 157 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-CP: DESIGNED SEO MUTATED AAS CONSENSUS-A | -?r???? .?-?i-?a?kqk-gd?.llkpk-y-EINgTke?-kqk-ke. HnqP?p | 331 360 344 344 65 321 306 157 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-CPS DESIGNED SEQ MUTATED AAS CONSENSUS-A CONSENSUS-B | -?r???? .?-?i-?a?kqk-gd?.lltkpk-y-EINgTke?-kqtekke. HqP?p | 331 360 344 344 65 321 306 157 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-G CONSENSUS-G CONSENSUS-O CONSENSUS-U CONSENSUS-CP: DESIGNED SEQ MUTATED AAS CONSENSUS-A CONSENSUS-B CONSENSUS-C | -?r???? .?-?i-?a?kqk-gd?.lltkp | 331 360 344 344 65 321 306 157 |
| CONSENSUS - D CONSENSUS - E CONSENSUS - G CONSENSUS - H CONSENSUS - O CONSENSUS - O CONSENSUS - C DESIGNED SEQ MUTATED AAS CONSENSUS - A CONSENSUS - A CONSENSUS - C CONSENSUS - C CONSENSUS - C CONSENSUS - D CONSENSUS - B | -?r???? .?-?i-?a?kqk-gd?.llkp | 331 360 344 344 65 321 306 157 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-CP DESIGNED SEO MUTATED AAS CONSENSUS-A CONSENSUS-B CONSENSUS-C CONSENSUS-C CONSENSUS-D CONSENSUS-B CONSENSUS-B CONSENSUS-B | -?r???? .?-?i-?a?kqk-gd?.llkp | 331 360 344 65 321 306 157 355 374 366 361 398 372 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-CP DESIGNED SEQ MUTATED AAS CONSENSUS-A CONSENSUS-B CONSENSUS-C | -?r???? ?-?i-?a?-kqk-gd?.lltkpk-y-EINgTke?-kqtek-ke. HqP?p | 331 360 344 65 321 306 157 355 374 366 361 398 372 373 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-CP DESIGNED SEQ MUTATED AAS CONSENSUS-A CONSENSUS-B CONSENSUS-F CONSENSUS-G CONSENSUS-H | -?r???? ?-?i-?a?-kqk-gd?.lltkp | 331 360 344 65 321 306 157 355 374 366 361 398 372 373 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-CP DESIGNED SEQ MUTATED AAS CONSENSUS-A CONSENSUS-B CONSENSUS-C | -?r???? ?-?i-?a?kqk-gd?.llkpk-y-EINgTk-e?-kqtek-ke. HnqP?p | 331 360 344 65 321 306 157 355 374 366 361 398 372 373 92 356 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-CP DESIGNED SEQ MUTATED AAS CONSENSUS-A CONSENSUS-B CONSENSUS-F CONSENSUS-G CONSENSUS-H | -?r???? ?-?i-?a?kqk-gd?.llkpk-y-EINgTke?-kqtek-ke. HnqP?p | 331 360 344 344 65 321 306 157 355 374 366 361 398 372 373 92 356 336 |
| CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - G CONSENSUS - O CONSENSUS - O CONSENSUS - C DESIGNED SEQ MUTATED AAS CONSENSUS - A CONSENSUS - B CONSENSUS - D CONSENSUS - B CONSENSUS - F CONSENSUS - G CONSENSUS - G CONSENSUS - H CONSENSUS - O | -?r???? ?-?i-?a?-kqk-gd?.llkpk-y-EINgTke?-kqtek-ke. HnqP?p | 331 360 344 65 321 306 157 355 374 366 361 398 372 373 92 356 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-G CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-C DESIGNED SEO MUTATED AAS CONSENSUS-A CONSENSUS-B CONSENSUS-B CONSENSUS-B CONSENSUS-C CONSENSUS-F CONSENSUS-F CONSENSUS-G CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O | -?r???? ?-?i-?a?kqk-gd?.llkp | 331 360 344 65 321 306 157 355 374 366 361 398 372 373 92 356 336 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-G CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-C DESIGNED SEO MUTATED AAS CONSENSUS-A CONSENSUS-B CONSENSUS-B CONSENSUS-B CONSENSUS-C CONSENSUS-F CONSENSUS-F CONSENSUS-G CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O | -?r???? ?-?i-?a?kqk-gd?.llkp | 331 360 344 65 321 306 157 355 374 366 361 398 372 373 92 356 336 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-G CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-C DESIGNED SEO MUTATED AAS CONSENSUS-A CONSENSUS-B CONSENSUS-B CONSENSUS-B CONSENSUS-C CONSENSUS-F CONSENSUS-F CONSENSUS-G CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O | -?r???? ?-?i-?a?kqk-gd?.llkp | 331 360 344 344 65 321 306 157 355 374 366 361 398 372 373 92 356 336 |
| CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - H CONSENSUS - O CONSENSUS - O CONSENSUS - O CONSENSUS - C DESIGNED SEQ MUTATED AAS CONSENSUS - B CONSENSUS - C C CONSENSUS - C C C C C C C C C C C C C C C C C C C | -?r???? ?-?i-?a?-kqk-gd?.llkpk-y-EINgTke?-kq- tek-ke.H- nqP?pk-y-EINgTke?-kq- tek-ke.H- nqP?p | 331 360 344 344 65 321 306 157 355 374 366 361 398 372 373 92 356 336 |
| CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - H CONSENSUS - O CONSENSUS - O CONSENSUS - C DESIGNED SEQ MUTATED AAS CONSENSUS - A CONSENSUS - B CONSENSUS - C C CONSENSUS - C C CONSENSUS - C C CONSENSUS - C C C C C C C C C C C C C C C C C C C | -?r???? ?-?i-?a?kqk-gd?.llkp | 331 360 344 344 65 321 306 157 355 374 366 361 398 372 373 92 356 336 |
| CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - H CONSENSUS - O CONSENSUS - O CONSENSUS - O CONSENSUS - C DESIGNED SEQ MUTATED AAS CONSENSUS - B CONSENSUS - C C CONSENSUS - C C C C C C C C C C C C C C C C C C C | -?r???? ?-?i-?a?-kqk-gd?.llkpk-y-EINgTke?-kq- tek-ke.H- nqP?pk-y-EINgTke?-kq- tek-ke.H- nqP?p | 331 360 344 344 65 321 306 157 355 374 366 361 398 372 373 92 356 336 |
| CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - H CONSENSUS - O CONSENSUS - O CONSENSUS - C DESIGNED SEQ MUTATED AAS CONSENSUS - A CONSENSUS - B CONSENSUS - C C CONSENSUS - C C CONSENSUS - C C CONSENSUS - C C C C C C C C C C C C C C C C C C C | -?r???? ?-?i-?a?-kqk-gd?.llt-kpky-EINgTke?-kqtek-ke. Hn | 331 360 344 344 65 321 306 157 355 374 366 372 373 92 373 92 356 336 175 |
| CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - H CONSENSUS - O CONSENSUS - O CONSENSUS - O CONSENSUS - C DESIGNED SEQ MUTATED AAS CONSENSUS - A CONSENSUS - A CONSENSUS - B CONSENSUS - C CONSENSUS - E CONSENSUS - F CONSENSUS - F CONSENSUS - F CONSENSUS - H CONSENSUS - H CONSENSUS - H CONSENSUS - U CONSENSUS - CPZ | -?r???? ?-?i-?a?-kqk-gd?.llt-kpky-EINgTke?-kqtek-ke. Hn | 331 360 344 65 321 306 157 355 374 366 361 398 372 373 92 356 336 175 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-O MUTATED AAS CONSENSUS-A CONSENSUS-A CONSENSUS-B CONSENSUS-B CONSENSUS-B CONSENSUS-G CONSENSUS-F CONSENSUS-F CONSENSUS-F CONSENSUS-G CONSENSUS-G CONSENSUS-G CONSENSUS-O | -?r???? ?-?i-?a?k | 331 360 344 344 65 321 306 157 355 374 366 372 373 92 356 336 175 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-O MUTATED AAS CONSENSUS-A CONSENSUS-B CONSENSUS-B CONSENSUS-B CONSENSUS-G CONSENSUS-F CONSENSUS-F CONSENSUS-G CONSENSUS-B CONSENSUS-G CONSENSUS-B | -?r???? ?-?i-?a?k | 331 360 344 344 65 321 306 157 355 374 366 361 398 372 373 92 373 92 375 |
| CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-O MUTATED AAS CONSENSUS-A CONSENSUS-A CONSENSUS-B CONSENSUS-B CONSENSUS-B CONSENSUS-G CONSENSUS-F CONSENSUS-F CONSENSUS-F CONSENSUS-G CONSENSUS-G CONSENSUS-G CONSENSUS-O | -?r???? ?-?i-?a?-kqk-gd?.llt-kpky-EINgTke?-kqtek-ke. Hn | 331 360 344 344 65 321 306 157 355 374 366 372 373 92 373 92 356 336 175 |

FIGURE 10 (Cont)

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| | ^^^ | | gp120 / gp4 | 1 |
|----------------------------|---|------------------------|------------------|------------------------|
| | TPRPGGGD I KDNWRSELYKYK | WKIRDIAWADTR AKRRVV | EREKRA VG | IGAMI FGPLGA |
| DESIGNED SEQ | I NMR | EK I K | | L FL |
| MULATED AND | - | • | _ | |
| Consensus-A | ?netFrPgGgdmrdNWrsELYkYl | (vVkiePlGvaPtr.akrRV | VeREKRA??vg | .lGavflgflGa 46 |
| CONSENSUS-B | -t-i | ·k | g | ?im 48 |
| CONSENSUS-C | -? | ·e-k? | -?? | ?i 47 |
| CONSENSUS - D | | ·r | I | m 46 |
| COMSENSUS-E | NiK | Qi | | .IMif 50 .?l 47 |
| CONSENSUS-F | -?n-k | eq | K | .? 40 |
| CONSENSUS-G | -?V | x | · | -? 18 |
| CONSENSUS-H | -?Vk-ITf | | | MLv-S- 46 |
| CONSENSUS-0 | ?-1?K-1TE | | 2 | M? 43: |
| CONSENSUS-U | | | 777.7-07?- | ?-???-?- 22 |
| CONSENSUS-CP | • | | | |
| NEGT/SED SED | AGSTMGAASITLTVQARQLLSGIVQ | QQSNLLRAI BAQQHLLQLTV | wgi koloarvlaver | YLKD QKPLG |
| MUTATED AAS | M L | ·N M | Į, | \mathbf{Qr} |
| FRG17122 1-1- | | _ | | |
| CONSENSUS-A | AGSTmGAaSiTLTvQarqLlSGIV | qqQsNllrAIeaQqhlLkLT | vngi kolqarvlave | xYLrD.QQLLG 531 |
| CONSENSUS-B | | n <u>q</u> | | k-? 548 k 539 |
| CONSENSUS-C | | m-Q | | k 533 |
| CONSENSUS-D | | NQ | | KKf 577 |
| CONSENSUS-E | ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~ | | | ? 546 |
| CONSENSUS-F | V | | | ? 549 |
| Consensus-G Consensus-H | | ??? | | 227 |
| CONSENSUS-0 | ATatht-?K | DO?R-S | RRLL-1 | rliQNn 529 |
| CONSENSUS-D | | N | | ES 496 |
| CONSENSUS-CPZ | ????-?-?-?- | ???Q-S | ?V? | ???-? 279 |
| | *** | | *** | |
| | | | | - |
| | LNGCSGKIICTTAVPNNSSN | S NKSLEBIWNNMTWM | EWEREISNYTNOIYE | ILTESQNQQ · |
| | I L N T | F D I | | |
| HOIMILD | - | | | |
| CONSENSUS-A | INGCSGKLICETnVPWNsSW | S.Nks??dIWdnMTWl | gWdKEisnYT?iIY? | .LiEesqngQ 586 |
| CONSENSUS-B | | ?1-??u | xe-erd1t | ?-L-d 603 |
| CONSENSUS-C | b | | | 589 |
| CONSENSUS-D | LIAt | | E-ERUGIS | .ILT 636 |
| CONSENSUS-E | L | Re?M | E-eSnER | ? 603 |
| CONSENSUS-F | t | fnEI | e-eRNqn | 1? 606 |
| CONSENSUS-G CONSENSUS-0 | 1 Y V-S-K71-7G | ???neS?L0 | gg-n-vss?e | .e-Q?A-? 500 |
| CONCENTETE -11 | Y | LVTLLM | ERQVG | L-DK 555 |
| CONSENSUS-CPZ | L??-??-7-TN????? | ?????.?????-? | ??LV?-?-G?-?- | .?L??A?? 312 |
| | • | | | |
| | | | | \/ 3'sj |
| | RNEQELLELDKWASLWNWFDITHNL | NYTYTOTHTUCCI.YCI.DTVP | AUT.STVNRVROGYSP | LSFOTLLPA |
| | KD A N SK | v i | I | T |
| MUTATED AAS | | _ | | • |
| CONSENSUS-A | EKNEGGLLaLDkWanLwnWPdIsnW | LWYITIPimIVGGLIGLRIV | faVlsiInRVRqGYS | PlSFQtltp? 655 |
| CONSENSUS-B | ?-t | kv | V | :T-9 P\T |
| CONSENSUS-C | bi | k i : | Vv | Б64 |
| CONCENTERE D | s-T? | k | 1V | 1-a 657 |
| ACCIONICATO - P | DDYDST | K i | V | p?Hh 705 |
| CONCENEUS - P | eS | K | VK | ?hi-S 672 |
| CONTORNICTIC - C | | k | V | ?ḤH 674 L-IP??h 647 |
| CONSENSUS-0 | K?EESilTK | K-A-IAV-Vi | ATNTAKNIÖ. | L-IP??n 647 |
| CONSENSUS-U | S-KBSG-T | К | -T-F | ?-????- 355 |
| CONSENSUS-CPZ | -?-???-?B?-?ST? | K?-?-?1?? | ::::-::K:: | .= 333 |
| | <- tat cds | • | | |
| * | | | | |
| DESTGNED SEO P | RG PDRPEGIEEEGG EQDRDRSVRI | VSGFLALAWDDLRSLCLFS | YHRLRDLILI A AR | IVELLGHS |
| MUTATED AAs | LGR RG G | ns <u>n</u> | F V | T R |
| | · - | - | | |

FIGURE 10 (Cont)

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| CONSENSUS - O CONSENSUS - U CONSENSUS - CP | q?E.agT-G- GG Z Q??????E | T | E-NN | VN | | E | I | | L | .v | K | G-R | 702 685 398 |
|--|--------------------------------|--------------|--------|-------|-------|---------|---------|--------|-------|-------|-------|-------|-------------------|
| | | | | | | <- rev | cds | | | | | | |
| DESIGNED SEO | SLRGLRRG | WEAL | KYL WN | LLQYW | GQELK | ISAVSLI | NATAIA | VAEGT | DRVII | EVAQI | ragra | ILHI | |
| MUTATED AAS | K Q | G | M G | L | L | NI | | GN | I | v | W | N | |
| CONSENSUS-A | slkglrlg | weg1 | kYL. w | Llly | grEL | C?SAinL | ldtiAia | avAgvt | DRVI | Sig(| rigRi | AilnI | 780 |
| CONSENSUS-B | ?:?? | a- | w | g | - sg- | -nvs- | -nat | Eg- | | -vv- | -a?- | h- | 789 |
| CONSENSUS-C | rqr | a- | Gs | py | -1 | ks- | | EG- | i- | -??- | ? | ? | 787 |
| CONSENSUS - D | R | | | | | | | | | | | | 773 |
| CONSENSUS-B | R | | Ġ- | | -Q | IS- | -naT | | | ~VA- | gaw | h- | 832 |
| CONSENSUS-P | .?RR | A- | -lG- | -t | -Q | Ns- | -N-Tv | Eq- | ?- | ?AL- | -? | | 787 |
| CONSENSUS-G | i | | | | | | | | | | | | 800 |
| CONSENSUS-O | li?y-gLWI | 1GQktIea | CR-c?A | v?Q | LQ~-q | nT | ?-V- | N | -qi- | lGi- | ?G | | 767 |
| CONSENSUS-U | | A- | G- | -V | -Q | NS | NATV | EG- | I- | -v | C | | 741 |
| CONSENSUS-CPZ | I-HSL | R~R~ | CTGG | 11Q | -K | IS | AT | EG- | I- | -AF- | VTL-I | -R | 460 |
| DESIGNED SEO | PRRI ROGLERAL | L | | • | | | | | | | - | | |
| MUTATED AAS | T P | _ | | | | , | | | | | | | |
| CONSENSUS - A | PrRIROGIBra | L1\$ | | | | | | | | | | | 793 |
| CONSENSUS-B | -? | | | | | | | | | | | | 801 |
| CONSENSUS - C | F-a- | -q- | | | | | | | | | | | 800 |
| CONSENSUS-D | -? | - <i>-</i> - | | | | | | | | | | | 785 |
| CONSENSUS - E | | ' | | | | | | | | | | : | . 845 |
| CONSENSUS - F | -?? | | | | | | | | | | | | 798 |
| CONSENSUS-G | | | | | | | | | | | | | 813 |
| CONSENSUS-O | ?- | | | | | | | | | | | • | 779 |
| CONSENSUS - U | P | | | | | | | | | | | | 754 |
| Consensus - CPZ | | | | | | | | | _ | | | | 473 |

| DESIGNED SE | Q MGGKNSKSSLVGNPEVRERI | ROT | PPAAEGVGAVS | QD LDKHG | AITSSNT | PA |
|--------------|------------------------|-------------------|----------------|---------------------|-----------------|-------|
| MUTATED AAS | | RA | A A | R Y | L ; | A |
| MUINTED IN | | | | _ | | • |
| ISOLATE-E | MGGKNSKSSIVGNPQVRBRI | KQT | PPAAEGVGAVS | Go ldkh e | avtssnm | |
| | | | | | | |
| CONSENSUS-A | MGGKWSKsSiVgWPeVrkRm | RqT | ?PLAAkGVGAvS | QDLDkhG | A1TSSNt? | ?? 41 |
| CONSENSUS-B | ?-?-?e | -ra?????????????? | | | | |
| ISOLATE-C | MGGTMSKCSPVGNPAIRERI | RRA | APAAEGVGAAS: | | altssnti | |
| CONSENSUS-D | AI-B-I | -x-????? | .dPD | RB | | as 50 |
| CONSENSUS-O | NA77-?KP???? | -R????P?· | ·?PC-P??-] | RBA?R-0 | G-?H-P | PQ 36 |
| CONSENSUS-U | ???????-E-I | -?-??? | -P????- | ?????-?-?- | -????A | i– 31 |
| | | | | | | |
| \vskip6pt | | - 1 1 1 1 0112 | binding | | | |
| | SH3-bindir | ng · SH3- | DINGING. | | | |
| DECTANDO CEC | NNADCVWLK AQE E EG | VGFPVRPQVPLRPMTYK | GAFDLSFFLKE | CGLEGLVYSKK | QEILDLW | v |
| MUTATED AAS | PAE E | | AV L | DIQ | D | |
| MOTATED MYS | r A B D | | | - | _ | |
| ISOLATE-B | NNADCVWLR AOR E EG | VGPPVRPQVPLRPMTYK | Gapdlspflker | GGLEGLVYSKK | QEILDLW | V |
| 130Enie | | | | | | |
| CONSENSUS-A | tnpsCaNLE?Age?.de?. | VGPPVRPQVPLRPMTYK | gavdlshflker | EGLDGLIYS?kR | GRITDIM | V 110 |
| CONSENSUS-B | ade??-e? | | a-? | e?-q | -d | - 108 |
| ISOLATE-C | NNPOCAWLE AGER E EE | VGFPVRPOVPLRPMTYK | aafdlslplkek | GGLEGLIYSKKR | ÖBI FDFM | 7 |
| CONSENSUS-D | | | e | BW-K | | - 115 |
| CONSENSUS-O | N-AAL-P-7.SH?? | ??- | ?-FF | ?H | A | ? 93 |
| CONSENSUS-U | N-??-???E?E. | | F? | ?? | | - 83 |
| CONSENSUS-0 | N-FF-::::E:E: | • | • • | | | |
| \wskip6pt | • | | | | | |
| (van-Pok- | _ | SH3-bindir | 19 | | | • |
| | · | * | | | ٠. | • |
| | • | | | | | |
| DESIGNED SEQ | YHTQGFFPDWHNYTPGPGIRY | | | CLLHPMSQHGMEI | YEEKEAPT | |
| MUTATED AAS | N Y Q T | S | AB | ICL. | D, K | • |
| | ν | | | | | |
| ISOLATE-E | YHTOGFFPDWHNYTPGPGIRY | PLCFGWCFKLVPVDPRE | VE EDNKGENNO | TLLHPMSQHG1E | DREKRATI | |
| | · | | | er r marconicosoft | - Irans - | 176 |
| CONSENSUS-A | Yntogefpdwonytpgpgtre | PLTFGNCEKLVPVDPAE | vk.eac?Genns | THE LOCATION OF | C: LCVIII | 174 |
| Consensus-B | -hy?-y | ?e-ex | ne | · | been sin a | |
| ISOLATE-C | YNTOGFFPDWONYTPGPGVRY | PLTFGWCFKLVPVDPSE | VE BINEGENNO | JUHPASIMISMEL | -DANADA | |
| CONSENSUS-D | II-Y | q- | Et-c | ;YB- | br-dx | . 182 |
| CONSENSUS-O | -??? | LS?E- | A-rignt?-?a? | 'X-??B- | ?H?-1-? | 150 |
| CONSENSUS-U | -H??-?-?-? | ???-?- | NC | :?S?- | ?E? | 138 |
| | • | | | | | |
| vskip6pt | | _ | | | | |
| | | • | | | | |
| | | ALD C | | | | |
| | WKFDSRLARRHIARBLRPEFY | KDC . | | | | |
| nutated aas | ньм нү | | | | | • |
| | *********** | VIVC | | | | |
| SOLATE-B | WKFDSALARRHIARELRPEFY | RDC | | | | |
| onomicite > | WkFDSrlalkHra?ElHPEfY. | rncs | | • | | 199 |
| | -rfh-m-ry | | CDENDIACTORIUS | RALECCY | | 230 |
| | | | "VPUNTOOT GDII | | | |
| SOLATE-C | WKFDSHLARRHMARELHPEYY | | | | • | 206 |
| ONSENSUS-D | -R-N fB-K-R-m | | | | | |
| ONSENSUS-O | -?RS-G?T-???LF? | -? | | | • | 166 |
| OMORNICHT IT | C22-2-D-22- | | | | | 157 |

FIGURE 11

GAG OVERLAPPING SEGMENTS

18/216

FIGURE 12 (Cont)

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| വ | aca agc | н⊳ | rto |
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| Ч Н | att | E | aca |
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| O. | 9 | [-1 | BCC |
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Segment 17

FIGURE 12 (Cont)

| 21 | 131 | • |
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| 41 | /21 | 6 |

| G D I Y K E E and ang G C R M Y Q G R M Y Q G R M Y Q G R M Y Q G R M A G C C C C C C C C C C C C C C C C C C | Segment 18 | Segment 19 | Segment 20 | Segment 21 | Segment 22 | Segment 23 |
|---|---|---|---------------|------------|---|--|
| A THE COC THE | PVGDIYK E ccc gtg ggc gaw atc tat aag | K I V R M Y Q S t asg att gtc agg atg tac yma | Q G P K E P F | KTLRAEQATO | MTETLLVQ D 3 atg aca gaw acc ctc ctg gtc co | SILKALGTGATLEEMMTACOGGGGPSH TRPR Wea att etg axa goc etc ggc mea ggc get wec etc gag gaa atg atg aca gcc tgt eag gga gtg gga ggc eet rgc gal |

| Segment 24 | Segment 25 | Segment 26 | Segment 27 | Segment 28 | Segment 29 |
|---|--|---|--|---|---|
| MMTACQGVGGPSHKARVLAEAMSQATHANI | RVLAEAMSQATHANIMMQRGNFKGOKRIIK | MMQRGNFKGQKRIIKCFNCGKEGHLARBCR | CFNCGKEGHLARNCRAPRKKGCWKCGKEGH | APRKKGCWKCGKEGHOMKDCTERQANFLGK | QMKDCTERQANFLGKIWPSNKGRPGNFPQS H S S caa atg aaa gac tgt acc gaa agg caa gcc aat ttc ctc ggc aaa atc tgg ccc tcc mrc aaa ggc aga ccc gga aac ttt cyc caa agc |
| G | VNN | RPV | IK | R | |
| atg atg acc get tgc caa ggc gtc ggc gga ccc rgt cac aaa gcc agg gtc etg gca gag get atg tec cag gyg amc mac get aac att | aga gig ctc. gcc gaa gcc atg agc caa gyc amc mat gcc aat atc atg atg cag aga ggc aat tto ara ggc cma aag aga atc rtc aaa | atg atg caa agg gga aac ttt arg gga cmg aaa agg att rtc aag tgc ttt aac tgt gga aag gaa ggc cat mtc gct arg aat tgc aga | tgtttc aat tgc ggc aaa gag gga cac mtt gcc axa aac tgt agg gcc cct aga aag aaa ggc tgt tgg aaa tgc gga axg gaa ggc cat | gct ccc agg aaa aag gga tgc tgg aag tgt ggc ara gag gga cac cag atg aag gat tgc aca gag aga cag gct aac ttt ctg gga aag | |

FIGURE 12 (Cont)

| | | | | | | 23 |)/. |
|---------------------------|---|------------------|---|----------------------------------|---|-----------------------|---|
| Segment 30 | | Segment 31 | | Segment 32 | | Segment 33 | |
| EN FOFO | tee arg eet gag eet ace get eee eet gee gaa are tit rga tte gge | ETTPSPKQEQKDKE | tto gga gag gaa acc aca cco tco cma aag caa gag cma aag gat aag gag | OKDKEHYPPSASLKSLFGND 1. 1. 1. | aag toc otg ttt ggo aat gac | | |
| сиғрозкрерт.дррд. г. я | ר שכם שמד סכם כסד | 8 4 8 8 | a ccc tcc cma aag | SASL | cod cot tya god ago oto aag too otg ttt | | ø |
| 다 더 다 | g oot gag oot | E E E | g gaa acc ac | 다 다 가 | c tac ccc cci | и В О | c tva tcc ca |
| Q Q X X | rg cag tcc ard | ው ው ው | gg ttc gga ga | 区田田 | ac asa gaa cwc tac | L F G N D P L S Q S S | age ete tte aga aae gat eee tva tee eaa |
| A A Z | ggc aat ttc cyg cag | E E D D | gag art ttc rgg | E O N D | gaa cmg aaa gac | ន ក ភ | age ete tte g |
| ი გ | gga agg cct | P P A I | מכך מכם פכד | A A O | cmg aaa cag | S L K | ccc tva qct toc ctq aaa |
| ა 2 ස : 2 | S cct age mrc aag | EPTA | gaa ccc aca gcc | E E | aca acc cct ago | P P S A | act ace twa get |
| H ⊠ | att tgg c | 以 5 日 | 000 | ы ы | ਰੁਵਣ ਤੁਕਤ ਕ | 田山 | CWC tat cct |

POL OVERLAPPING SEGMENTS

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| Segment 1 | Segment 2 | Segment 3 | Segment 4 | Segment 5 | Segment 6 |
|--|--------------------------------|---|---------------------------|---|---------------------|
| FFRENLAFQQGKAREFSSEQTGANSSASKK ttc ttt agg gaa amc ctg get ttc cmg caa ggc raa gcc aga gag ttt ycc agc gaa cac aca gct ttc cmg caa ggc raa gcc aga gag ttt ycc agc gaa cac aca gcc raa | GGAERQ D 99a 99c qqa qqq | GDGGGAERQGTSSS D 1990 gat 990 994 990 gct 9aw a99 caa 990 acc too ago too | C cet cag att acc ete tgg | T I I I I I I I I I I I I I I I I I I I | gac gat aca gtg ctc |

| Segment 13 | | Segment 14 | | Segment 15 | | Segment 16 | | Segment 17 | |
|---|--|--|---|--------------------------------|---|---|---|------------|---|
| LTEICKEMBEEGKISKIGPENPYNTPVFAI A T K R R I I I I I I I I I I I I I I I I I | ctc acc gmg atc tgt ama gaa atg gaa vaa gaa ggc aaa atc tcc arg att ggc cct gag aat ccc tat aac aca ccc rtc tt gcc att | K I G P E N P Y N T P V F A I K K K D S T K W R K L V D F R R | arg ato gga cco gaa aac cct tac aat acc cct rtc ttc gct atc aag aaa aag gac tcc acc aaa tgg aga aag ctc gtg gat ttc aga | KKKDSTKWRKLVDFRELNKRTQDFWEVQLG | aaa aag aaa gat agc aca aag tgg agg aaa ctg gtc gac ttt agg gag ctc aac aaa agg aca cag gat ttc tgg gag gtc cag ctc ggc | E L N K R T Q D F W E V Q L G I P H P A G L K K K K S V T V | gaa ctg aat aag aga acc caa gac ttt tgg gaa gtg caa ctg gga atc cct cac cct gct gga ctg aaa aag aaa aag tcc gtg aca gtg | 6-1 | K D att occ cat occ god ggd otc aag aaa agd gtd acd gtd otg gat gtg gga gad gdd tad ttt agd gtd occ otd gad raa rro |
| | | | | | - | | •• | • | • |

Segment 18 Segment 20 Segment 21 Segment 22 gag cct cag gga tgg tcc atg mcc maa atc ctc EMVIYQYMDDLYVGSDLEIGQH D cot gas atg gto ato tat cag tat 闰 ⋈ Ц Z O $\boldsymbol{\vdash}$ Z O X O HE Д gge att agg tat cag tat aac gte etg Ŋ atc cct Д Σ ល att ttc caa agc Z Н ВΩ Ŋ 808 بخ Н Q Д aga aag tat acc get tte Ø K [I, ſτι z FRIKN KQ ttt agg awa maa s ø Н **₹**₽ E 吆 CCC ≻ Н Д gga tcc × O Ŋ gat gag cct P4 Д PSINNETP
T
Tccc tcc ayc aat aac gaa acc co Ö Д ttc atc aga tac caa tac aat gtg ctc ccc caa ggc tgg aag [z, ¥ 凶 SMTKILE PQ DESI ⋈ Ö Q tcc gtg cct ctg Ы Д Д Ы > > acc att toc Ŋ Н 2 Ŋ PAIFOS (P) cot set ate ttt cag t tto aat ccc ſτι H >4 Д tat gcc ttt × Ī4 Q Z X Over Z, K ⋈ gat aca H X g Ω H P. tac aga Ö Þ Н œ **99a** ttc > × O Ŋ ſĽ, CCC **3**3c S R Д Q Д ACB Ы ſτι Н × 闰

| Segment 23 | | Segment 24 | | Segment 25 | | Segment 26 | • | Segment 27 | |
|---|--|-------------------------------------|--|--------------------------------|---|-------------------------------------|--|-------------------------------------|--|
| M D D L Y V G S D L E I G Q H R T K I E E L R A H L L R W G A E K | Q atg gat gac ete tae gte gge tee gae ete gag att gge eaa eae agg ree aaa ate gaa gag ete agg sma eae ete etg ara tgg gga | RTKIEELRAHLLRWGFTTPDKKHQKEPPFL A | 💭 aga rca aag att gag gaa ctg aga smg cat ctg ctc ara tgg ggc ttc aca acc cct gac aaa aag cat cag aaa gag cct ccc ttt ctg | FTTPDKKHQKEPPFLWMGYELHPDRWTVQP | ttt acc aca ccc gat aag aaa cac caa aag gaa ccc cct ttc ctc tgg atg gga tac gaa ctg cat ccc gat agg tgg acc gtc cag cct | WMGYELHPDRWTVQPIELPEKDSWTVNDIQ V | Q tgg atg ggc tat gag etc cac ect gae aga tgg aca gtg caa ece ate 84g etc ece gaa aag gas tee tgg aca gtg aat gae att eag | IELPEKDSWTVNDIQKLVGKLNWASQIYAG V | Q att BWG ctg cct gag aaa gaw agc tgg acc gtc aac gat atc caa aag ctc gtg gga aag ctc aac tgg gcc tcc cag att tac acc gga |
| | | | | | | | | | |

| L K T G K Y S R K R S A H T N D V R Q L T E V V Q K T A A ctc asy acc ggc ast tack tet agg avg agg rgg ggc cat acc ast gac ctc arg cas cag gac gro ast agg it gcc act acc ast gac ctc arg cas crg aca gac grt ggc ast agg it gcc act acc ast gac ctc arg cas crg aca gac grt ggc ast agg it gcc act acc ast gac ctc arg cas crg aca gac grt ggc ast agg it gcc act acc ast gac ctc arg acc gac agg acc at ggg as agg acc at ggg acc acc ast tc gct acc gas agg acc at ggg acc acc ast tc acc acc ast tc acc acc acc acc acc acc acc acc acc |
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FIGURE 12 (Cont)

FIGURE 12 (Cont)

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| Segment 51 | Segment 52 | | Segment 53 | | Segment 54 | | Segment 55 | | Segment 56 | |
|---|--------------------------------|--|--------------------------------|---|--------------------------------|--|------------|---|------------|-----------|
| Q L K G E A M H G Q V D C S P G I W Q L D C T H L E G K V I I N I caa ctg aaa ggc gaa gcc ats cat ggc caa gtg rat tgc tcc ccc ggc att tgg caa ctg gat tgc aca cac ctc gag gga aag rtt atc | GIWQLDCTHLEGKVILVAVHVASGYIEAEV | L gga atc tgg cag ctc gac tgt acc cat ctg gaa ggc aaa rtc att ctg gtc gcc gtc cac gtc gcc tcc ggc tac att gag gct gag gtc | LVAVHVASGYIEAEVIPAETGQETAYFLLK | 1. cto gig got gig cat gig got ago gga tat ato gaa goo gaa gig ato oot goo gaa aco gga cag gaa aco got tao tit mio eto aag | IPAETGQETAYFLLKLAGRWPVKVIHTDNG | L 'I' att ccc gct gag aca ggc caa gag aca gcc tat ttc mtt ctg aaa ctg gct ggc aga tgg cct gtg ara ryc att cac aca gac aat ggc | VKAACWWA | K. 1. T. T. Ctc gcc gga agg tgg ccc gtc arg rya atc cat acc gat aac gga agc aat ttc aca agc rct rcc gtc aag gct gcc tgg tgg gct | AVKAACWWA | t gtg aaa |

FIGURE 12 (Cont)

| Segment 57 | | Segment 58 | | Segment 59 | | Segment 60 | | Segment 61 | | Segment 62 | |
|-----------------------|---|-------------|--|------------|--|------------|--|-----------------|---|-------------------|--|
| ט | tat aac oot cag too cag ggo gto gtg gaa ago atg aac aaa gag oto aag aaa ato att ggo | Σ | D a ctg aaa aag att atc gga cag gtc agg gam cag gct gag cat ctg aaa acc gct gtg caa atg | ტ | R aag aca gcc gtc cag atg gcc gtc ttc att cac aat ttc aaa agg ara ggc gga atc gga ggc | н | $\langle \mathbf{K} angle$ aga arg gga att gga gga tac tac gaa gag aga atc x tt gaa att ata got asa gat atc | ſτ _ι | كال كا gat atc att gcc wcc gac att cag tat aag gaa ctg caa aas caa atc mya aag att cag aat ttc | Д | Γ att myc aaa atc caa aac ttt agg gtc tac tat agg gat agc aga gac cct mtc tgg aag gga ccc |
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| 闰 | gag | H | | ድ | 386 | Д | gac | н | a ato | А | 986 |
| × | 888 | 田 | g cat | × | 388 | н; | > '; | O | 8 8 8 | œ | 96 1) |
| YNPQSQGVVESMNKELKKIIG | 3 aac | 闰 | D B S | FKRKGGIGG | n t t | н | a ate | LOKOITKION | Z 88 | QNFRVYYRDSRDPIWKG | n ga g |
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| zu | H | ט | g | O | CBB | Ø | gat | ≯ | tat | Ø | 880 |
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| Segment 63 | | Segment 64 | Segment 65 | | Segment 66 | |
|-------------------------|---|--|---|---|-------------|---------------------------------------|
| PIWKGPAKLLWKGEGAVVIQD : | L) ccc mtt tgg aaa ggc cct gcc aaa ctg ctc tgg aaa ggc gaa ggc gct gtg gtc atc caa gac | AVVIQDNSDIKVVPRRKAKII gcc gtc gtg att cag gat aac tcc gac att aag gtc gtg cct agg aga aag gct aag att atc | R K A K I I R D Y G K Q M A G D D C V A G | agg aaa goc aaa ato att agg gat tao gga aag caa atg got ggo gmt gao tgt gtg got rgo | DDCVAGRQDED | Ų |
| H | la cto | Ðğ | × | at tag | Д | aa qa |
| X | 8 | ល ភ្ | О | 36 BE | Q | ğ |
| 4 | ct g | at a | K | t B | 124 | . U |
| <u></u> | Ö S | Ο g. g. | H | tc a | ט | ដូ |
| <u> </u> | 8 8 9 | Ct o | H | रा स | A; | ב ב |
| ~ | ρί ρι ες | T H | ×4 | ν. Σ | ;> :> | : د |
| . | 1 t | rtc 9 | K4 ~ | 5 881 | 0 | ac t |
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| | | 5 2 998 | 14 | 8 B B | | A DEC |
| i ~⁄ | agg gat | E C | Д | טטט | Ů √ | č t |
| .v | 8 | | > | atc o | 7 | ata o |
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| ન ૪ | aga gac tcc | N 3 | X V | 888 | 8 4 | 989 |
| - | 283 | 15 tg 1 | | atc aaa gtg gtc | לי | 40 |
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| > | atg 1 | 7. ₹8. 8. 8. 8. 8. 8. 8. 8. 8. 8. 8. 8. 8. 8 | ຜ | Bgc (| DYGKQ·MA | a t t |
| K V Y Y K U S K D | aga gtg tat tac | AKLLWKG gct aag ctc ctg tgg aag ggs | N S D | aat agc gat | 124 | 9 |
| - | - | | | | | |

VIF OVERLAPPING SEGMENTS

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| Segment 1 | | Segment 2 | Segment 3 | Segment 4 | Segment 5 |
|---------------------------------------|---|--|--|--|--|
| IVWQVDRMRIRTWNSLVKHHMY Segment 1 K | agg aca tgg aaw agc ctc gtg aaa cac cat atg | LVKHHMYISKKAKGWFYRHHYE Segment 2 H Ctg gtc aag cat cac atg yac atc tcc aag aaa gcc aaw ggc tgg ttc tat agg cat cac twt gas | FYRHHYESQHPKVSSEVHIPLG Segment3 FDR | GEARLVIRTYWGLQTG Segment4D I K H H H H H H H H H H H H H H H H H H | YWGLQTGEKDWQLGHGVSIEWR Segment 5 H tat t99 99a ctg caw acc 99a 9ag ara 9ac t99 cas ctc 99c caw 99c 9tc agc att 9ag t99 agg |
| R L | atg arg att | S | Q K g | A E | ⊠ R a l |
| Σ | g atg | C atc | လ နွ | 田口幣 | 西 . B |
| œ | atc gtc tgg caa gtg gat agg | > H ½ | ыOg | PLG cet cetg gg | ည ^{ရွိ} |
| А | 6. 6. | E a I | 발표 | EVHIPL | () ¥ |
| > | ai Gt | Η Β 1 | H g | <u>Ω</u> , δ | (a) III & |
| O | <u> </u> | LVKHH CTG GTG GAT CBI | FYRH tt tac aga cac | EVHI gaa gtg cat at | ᆸ |
| 3 | a tg | N 26 | 요 . | ដ្ឋា | ည် ရှိ (၁) |
| > | c gt | g gt | t t | ₽ 9. | ئا د ج |
| Н | | | | | |
| ΣH |) mtg | Ω ± 00 00 00 00 00 00 00 00 00 00 00 00 0 | W tgg | လ နို | E B |
| > | gtg | Z X s | ධ _{කුළි} | ល ដូ | 况 X g |
| Ø | 8 | ¥ tgg | X Z ss | V gtg | at H |
| Z | tgg | E S | A get | ₹ Sass | > H # |
| R | aga aga | 다 gg gg | X 88 9 | വ | ctg |
| Z | 8 | H # | ₩ | H cat | 저 🖁 |
| 闰 | ಷ ಪ | $\mathbf{x} \mathbf{x}_{\mathbf{z}}^{\mathbf{z}}$ | လ စ္အီ | O R E | ₹ |
| Σ | atg | A tg | H # | လ ဗို | 田口幣 |
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Segment 10 gga cac aat aag gtc ggc tcc ctg caa tac ctc gcc ctc gtg agm agg aga tgc gaa tac cct aag aaa atc ara ccc cct ctg cct agc gat cae ago rea ate OE Ы ß Н ď Д 闰 Д 900 Ы Ø O Н ഗ tgc ttt kcc gat gae cet gre ete × Д Н Ω 召 O വ വ Д 民 SA Ы 民民 Д Γı വ А U > Н gat tat age aca cag gte gga cas aka > Ω нα Ü K tat ttc ĸ > Ø بحرا OH ¥ Qι Н × Ö aga gcc att ctg gtg gga agc ctc cag tat ctg gct ctg amg gct ctg att amg ctc yas ؤ(≻) EH X z ഗ Н H Ы н × Н **ags** C B C ט Ы ď, **84 03** 耳 ល ។ ភ្នំ aaa Ø 노 R Н Y P Q Can att agg aga mwg gac caw ctg X F 姳 Q T K Ы OH Ы н ፈ gag t99 rcc A, HK 闰 Ω 3 got agg tgt atc gaa ы U Z, ល 闰 gac × Ы 吆 А Н ton grt tte ket R Ø D G SA ß gtg **ജ** വ ജൂ Н > Д [I, tgt gtc **9**98 > Д ഗ U Ö CaB H Kk Ag 丑 O > Ω Ü 99a ttt OH & Caa O > r Į, Н × Ü X Ы Caw tcc уак got atc ctc Ø K H O Н Z OH tgg tac 耳 ⋈ ⋈ Ы Н gat cat Ö വ വ 耳 ø Д S & X K × Н α P Q 6 ĸ O T K Ы 闰

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| Segment 11 | | Segment 12 |
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VPR OVERLAPPING SEGMENTS

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| Segment 5 | | Segment 6 | |
|----------------------------|---|--------------|---|
| SRIGILRORRAR I G | rtt cac ttt agg att ggc tgc crg cac tcc agg att ggc att myc aga cag aga agg gsc aga | | |
| ын E | att myc aga | | |
| D D | att ggc | ശ | toc |
| cz Cz | tcc agg | ι Σ | tec agg |
| O K | crg cac | | а99 саа адд ада двт адд аас дда ксс тсс адд тсс |
| и С С В В В | ggc tgc | 8 8 8 | agg aac |
| н | agg att | Q R R Q G | g aga gat |
| E H | cac tt | O M | g caa ag |
| H > | ttc | H H R | myc |
| 디 | g ctc mt | ъ Б | gga at |
| л 0 0 | g caa ca | PI pri | c aga at |
| H H | att agg ayc ctg caa cag ctc mtg | H S | cra cat age aga ate gga ate |
| H K | att ag | r Ork | tgt cr |

TAT OVERLAPPING SEGMENTS

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| Segment 1 | | Segment 2 | | Segment 3 | | Segment 4 | | Segment 5 | |
|-----------|---|---|---|---|---|---------------|--|----------------------|---|
| КСҮСККО | atg gaw cyc gic gac cet aas ete gag eet igg aaw cae eet gge tee eag eet amg aea gee igi wme aaa ige iai ige aaa aag ige | SQPTTACSKCYCKKCCFHCQLCFLKKGLGI Seg K T Y V T T N | ago caa oco ama aco got tgo wmo aag tgt tao tgt aag aaa tgt tgo two cao tgt cag sto tgo tto otg ama aag gga otg gga ato | 2 2 3 4 5 4 5 7 7 | . cat tgc caa stg tgt ttt ctc amg aaa ggc ctc ggc att agc | алаоватахона. | 나 기다 가 다. 그 이 교육 영영 arg caa agg aga agc gcc cct cag agc agm rag gat cac caa tac cc | EQPLPQTRGGNPTDPKESKK | S P D G E $_{ m c}$ cag gac cat cag tat ccc att ycc gaa cag cct ctg yct cag mca agg gga grc aat ccc aca grc cct rag gaa agc aaa aag |
| | | | | | | | | - | - |

Segment 6

FIGURE 12 (Cont)

QTRGGNPTDPKESKKEVASKTETDPCD PDA GERCCC raa gag tcc aag ata rag gtc gmg tcc aag aca gac cct tkt gac

different

REV OVERLAPPING SEGMENTS

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FIGURE 12 (Cont)

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| Segment 6 | | | Segment 7 | • | | Segment 8 |
|---|---|---|-----------|----|--------------------------------------|-------------------|
| ט | | acc tcc ggc aca cag caa agc caa ggc aca gag aca gga gtg gga | ט | | 998 | |
| > | | gtg | Д | ß | Ycc | |
| ט | | 998 | υ | | 265 | |
| H | | 8 0 8 | Ы | | C to | |
| 闰 | | gag | Н | > | rtc | |
| [⊣ | | aca | SVILGP | Æ | gyt | |
| ט | | 996 | ຜ | | agc | |
| Q | | Caa | ഗ | | toc | |
| Ŋ | | agc | | | gag | |
| 0 A 0 H A H O O O O O O O O O O O O O O O O O | | Caa | <u>ភ</u> | | tyg gga, gag tcc age gyt ztc ctc ggc | |
| Ø | | 680 | യ | 니 | tyg | |
| Η | | 808 | Н | | cag att | |
| ტ | | 990 | Ø | | Cag | Z |
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| J | Ω | tgc tcc gag gat wgc grt | ტ ბ | | gtc ggc | ប |
| J | ഗ | ¥ | > | | gte | ው ወ |
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VPU OVERLAPPING SEGMENTS

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| Segment 1 | Segment 2 | Segment 3 | Segment 4 | Segment 5 |
|--|---|---|---|--|
| TPLEIIAIVAFIVALIIAIVVTIAYSES S Q R L L L L L A L Seg aca atc gct atc gtc gcc ctc atc mta gcc att gtg gtc tgg aca atc gyc twc att gag tat | IIAIVVWTIAYIEYRKLLRQRRIDRLIKR Seg L att mtc gct atc gtc gtg tgg acc att gyg twt atc gaa tac arg aaa ctg ctc arg caa agg ara atc gat agg ctc atc raa agg | K L L R Q R R I D R L I K R T R E R A E D S G N E S E G D Seg K K E I E I aag ctc ctg ara cag agt seg at rag aga ayc aga gag aga gcc gaa gac tcc ggc aat gag tcc gag gga gac | RERAEDSGNESEGDTEELSTMVDMGNYDL RAL agg gaa agg gct gag gat agc gga agc gat asa gaa gag ctc agc rca wtg gtc gac atg ggc aat tac gat ctg | TEELSTMVDMGNYDLGVDNNL R 88 gag gaa ctg tcc rcc wtg gtg gat atg gga aac tat gac ctc ggc gtc gac aat aac ctc |
| Z gt | L | 다(天) # # | E H & | E K g |

FIGURE 12 (Cont)

ENV OVERLAPPING SEGMENTS

| Segment 7 | | Segment 8 | | Segment 9 |
|----------------------------------|---|-----------------------|---|---|
| VEQMQEDVISLWDQSLKPCVK S D H I | g gig gam cag aig cam gaa gac rit aic icc cig igg gac caa agc cic aag cci igc gic aag | LKPCVKLTPLCVTLNCTNANL | tee etg aaa eee tgt gtg aaa etg aca eee ete tge gte ace ete aac tgt ace aat gee aat etg | |
| ы Н В | c rtt atc t | T G T | 9 aca ccc c | N V N |
| O H O H | cam gaa gad | V K L | gtg aaa cte | N L I |
| 版 (2) (3) (4) | gam cag atg | አ ው ር | aaa ccc tgt | N C T N A N L I N V N ast tgc aca age get age |
| > z Q | rac at | S S | cag | it g |
| Z | ttc aat atg tgg aag aat | S F S | age ete tag gat | L C V T] |
| | aat tto aat at | и п п | gat rtc att ag | L T P L |
| | | | | |

GAP IN SEGMENTS DUE TO HYPERVARIABLE REGIONS 1 AND 2

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| Segment 1 | Segment 2 | | Segment 3 | | Segment 4 | | Seement 5 | |
|--|-------------|--|---|--|----------------------------------|---|---------------------------------|---|
| YRLINCNTSVIKOACPKVSFDPIPIHYCTPPs SAT TITE AT A TATE AND A STAND ST | O Z L | CCC aaa rtc wcc ttc gam ccc att ccc at tgc rct ccc gcc gga twc gct atc ctc aag tgt aac rat aag amm ttc aat ggc | AGYAILKCNDKNFNGTGPCKNVSSVQCTHG S F T T T T | T got ggo twt gco att otg aaa tgo aat rac aaa ama ttt aac gga acc gga coc tgt amg aat gtg toc aac gto cag tgt aco cat ggo | TGPCKNVSSVQCTHGIKPVVSTQLLINGSL & | aac gtc agc wcc gtg caa tgc aca cac gga atc ara ccc gtc gtg tcc acc caa ctg ctc ctg aat ggc tcc ctg | IKPVVSTQLLINGSLAEEIIIRSENLTNN S | $V \ V$ V Set gic age aca cag etc etg etc aac gga age etc gec gaa gag gaa xte rit atc aga age gaa aac yit ace rat aac |
| | | | | | | | | |

FIGURE 12 (Cont)

FIGURE 12 (Cont)

Segment 7 AEEEIIIRSENLTINNAKTIIVHLNESVEIN (V)(V)

FDV

QKV

get gag gaa gat rit ric att agg tee gag aat yte aca rac aat gye aaa ace att ate gie cam ete aae raa age gie gwg att aae

| Segment 1 | Segment 2 | Segment 3 | Segment 4 | Segment 5 | Segment 6 |
|---|---|---|--|---|--|
| G G D I K D N W R S E L Y K Y K V K I E P L G V N M R 99a 99c rat ats ara gac ast t99 aga agc gaa ctg tat aag tat aag 9tc 9tg rag att rag cct ct9 99a rtc | KVVKIEPLGVAPTRAKRRVVEREKR E K I K | KRRVVERKRAVGIGAMIFGFLGAAA Q aag aga agg gtc gtg gaa agg gaa gcc gtc ggc mtt ggc gct atg wtt ytc gga ttc ctc ggc gct gcc | AMIFGFLGAAGSTMGAASITLTVQA FL 8 gcc atg wtc ytt ggc ttt ctg gga gcc gct ggc tcc atg ggc gct gcc tcc atg aca ctg aca gtg caa gcc | AASITLTVQARQLLSGIVQQQSNLL M gcc gct agc atk acc ctc acc gtc cag gct agg cwa ctg ctc agc gga atc gtc cag caa cag arc aat ctg ctc | GIVQQQSNLLRAIEAQQHLLLQLTVW N 99c att 9t9 caa cag caa axt aac ctc ct9 a99 gct atc 9aa 9cc caa cag cat mtg ctc cag ctc acc 9tc t99 |
| D & | ۲ tac | A Bot | agg g | ධ gg | ស ភ្ជុ |
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| R agg a | Kac t | T 3 | ට _{කු} | H BCB | the state of the s |
| t H | I H | Д 200 | V gtg | C Sg Sg | Q LI S |
| 9 H H | E G G G G G G G G G G G G G G G G G G G | A J | get 9 | D gg | 17 18 18 19 19 |
| | | | | | |

GAP IN SEGMENTS DUE TO HYPERVARIABLE REGIONS 3,4 AND 5

| Segment 7 | Segment 8 | | Segment 9 | ÷ | Segment 10 | | Segment 11 | | Segment 12 | ı |
|---|-----------|---|--|--|------------|---|------------|-------------------|------------------|--|
| RAIEAQQHLLQLTVWGIKQLQARVLAVERY M aga gcc att gag gct cag cag gag growth grown | IKQLQAR | gga atc aaa cag ctc cag gct agg gct rtc gaa agg tat ctg aaa gac caa mag ytt ctg gga mtc tgg ggc tgt agc gga aag | LKDOKFLGLWGCSGKIICTTAVPWNSSWSN OL I | 1 ytc ctc ggc mtt tgg gga tgc tcc ggc aaa mtc att tgc aca acc rmt gtg cct tgg aac ag | MMIMW | t atc tgt acc aca xmc gtc ccc tgg aat tcc asc tgg agc aat aag tcc | WEREISNYTN | t gag gaa atc tgg | IYEILTESONQODRNE | Lowg att tac raa atc ctc acc gaa agc caa aac caa cag gat agg aat gag |
| | | | | | - | | | | | |

agg rtt atc gaa gtg gyt cag Ö Q O Ø [I4 LGHSSLRGLRCG R K Q ctc 99° cxt agc tcc ctg ara 99° ctc crg aga tgc ctc tgg ggc cwg gaa ctg aaa awc tcc gcc rtt agc ctc ctg aat gcc aca aac ctc ctg cwa tat tgg **&** > 3 Н П α > U ď ctg aga arc ctc Ы Z 闰 Ы Ы Н S Z Н Н ᆸ 足 S Z œ н П Y L W N W W G I tat tkg kgg 8 gat gac ytt > H Ω 되도 Д ď Н Д Д G W : grg kgg **t**99 aga × ល ⋈ K EALKY G G gaa gsc ctc aag t ctc gcc aga ctg HZ ď Н ace get ate get gtg get × Ы П R 966 gaa ctg Ä Ы > K 出 ď 闰 × 闰 R I V E
T
Agg ayt gtg g tgg gga ttc O LI H Σį ſΞų Ŋ ctg ttt **9**8 ტ ტ ď Ü [14 **a**99 ctg gtc arc 3 PK Н S S Н A A I
V
syc get ctg tgt R Q E tee etg ete aac get \mathbf{c} ø > Ы П Z Н aga **88**8 gac ctc agg art ט ы $\alpha(z)$ H 24 gtg **スス**。 Ы Ы > α F gat ytc att ctc Ы Ы ഗ Н ß P4 О Ŋ > H toc Z, Д Ø А tac 田瓦路 × Ŋ D4 Z 吆 ម្ភិធ 888 gga × O HZ Ø Н ctg Q R E Н × Н α Н 二 Ы K Н 闰 n L × 闰 闰 Ċ 闰 tgg O L S tt > ⋈ Ö [ī, ល

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| Segment 25 | | Segment 26 | |
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NEF OVERLAPPING SEGMENTS

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| Segment 1 | Segment 2 | Segment 3 | Segment 4 | Segment 5 | Segment 6 |
|---|---|---|--|---|---|
| MGGKWSKSSLVGWPEVRERIRQTPPAAEGV Segatg gga gga gga gga gga gga gga gga gga | VRERIROTPPAAEGVGAVSQDLDKHGAITS Segote agge gate agge gate gye tee erg gat etg gat aag kae gga gee mte aee tee | TPANNADCVWLKA A P A E acc set gec aat aac set gac tgt gyc tgg etc rag get | SNTPANNADCVWLKAQEEEGVGFPVRPOPSegas accases of the segal coccession of the sega | QEEEGVGFPVRPQVPLRPMTYKGAFDLSFF Sega eas gag get cec ctg aga cet atg acc tac aas gag gre get ctg tec yte tte | LRPMTYKGAFDLS(F)FLKEKGGLEGLVYSKK Set ct agg etc atg acc at any gac ct agg ytg ttt ctg aca gag aca ggc gga ctg gaw ggc ctc rtc tat agc mag aca |
| | | | | | |

Segment 11 Segment 7 ctg tgg gtg tat mac aca cag gga two tgo ttt aag otc gtg oct gtg gat coc gtc Н EINKGENNCLLHPMSQHGMEDEEREV AE 938 ryc aat rag 9ga gag aat aac tgt ctg ctc cac cct ats rgt cwg cat 99c atg 9aa gac 9aa gas aga gag O 民 Ω Ы O H # > O Н Ö Д Z twt ttc cct gac tgg cas aat tac aca ccc gga ccc # Z Z 闰 × Ö Ы gtg gaa gag ryc aac raa ggc × Ŋ Д 以团 [±, Z Н U Ы × Z ctg gat tat ccc ctc acc ttt ggc tgg HK Ω z ⋈ Н HO 闰 Ö att Н ⊠ Œ, 闰 O E D > Д Н gaa Д Ы 闰 agg PR I വ് ſτι Д Д K Eq > × X Organ 990 gtc ccc gtc gac rya agg А Ö 民 toc CBB > ഗ O H H > gga ctg rtt tac **3**80 tgg gtc tac mat acc щ \vdash O Ы act > HZ p4 tgt ttc aaa ctg Н 口 × Ŋ caw aac tat acc cct ט > Д × 田口幣 3 H ſτι cta gat ctc Ы Ц ⋈ Ö 990 99a t9g O Ω Z ⋈ cag gaw atc ctc Ġ П HO Ü tto aag Н Z ſΞι 团 gaa ctg aca 臣(口) 闰 А H > 闰 Ø Ы Д aga ស ល ខ្លួ ttt Ы ĸ Д [z,

FIGURE 12 (Cont)

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| Segment 12 | Segment 13 |
|--|--|
| SOHGMEDEEREVLIWKFDSRLARRHIA CL rgc cwa cac gga atg gag gat gag gaa gtg ctg awa tgg aaa ttc gat agc crt ctg gct ckc agg cat ats gct | LIWKFDSRLARRHIARELRPEFYKDC K K H L M H Y |
| at B | Z Z |
| Δ | H X § |
| H g | i i |
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|----|-----|--|
| | | |
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| | ATC/ATT | | | 3/ATK | "/AWT | WTC/WTT | > | C/MTT | Z/AKT | T/AYT | C/RTT | > | | | | |
|------------------------------------|-----------------------------|--|----------------------------|----------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|--|
| | | | | | | | | | | | | | | | | |
| | I | | | H | Z | IF | H | 급 | 18 | H | 2 | ä | | | | |
| | CAC/CAT | | | MAC/MAT | SAC/SAT | CAM/CAN | CRC/CRT | CWC/CWT | CMC/CMT | YAC/YAT | | | | | | |
| | H Hs | Acids | | | | 웊 | | | | | | | | | | |
| | GGC/GGA | Amino | | KGG/ | GRC/GRT | KGC/KGT | GRG/GRA | GSC/GST | SGC/RGA | RGC/RGT | GKG/GKC | | | | | |
| | g gly | More | | 35 | 8 | ပ္ပ | B | S | g | g | ટ | | | | | |
| | GAA/GAG | TWO or More Amino Acids | | GAS/GAM | SAG/SAA | GMG/GMA | GRG/GRA | RAG/RAA | GWG/GWA | | | | | | | |
| | g]n C]n | For | | B | œ | Ø | ğ | Ä | à | | | | | | | |
| | CAG/CAA | Codons | | CRG/CRA | SAG/SAA | CAM/CAW | CWG/CWA | MAG/MAA | CMG/CMA | | | | | | | |
| | o gjn | rate | | | | F | | | | | | | | | | |
| Most Frequently Used Codons | C Q Cys TGC/TGT Gln CAG/CAA | Most Frequently Used Degenerate Codons | | | | KGC/KGT | | | | | | | | | | |
| 5 >- | აბ | Ω Y | | 3 | ទ | 8 | ່ບໍ | ဗ | ដ | | | | | | | |
| rednenci | D ABP GAC/GAT | requent] | | RAC/RAT | GMC/GMT | GAS/GAM | GRC/GRT | SAC/SAT | KAC/KAT | GWC/GWT | | | | | | |
| 78C | D ABI | OBt F | | No | ล | OR | ጀ | 占 | 20 | 8 | | | | | | |
| | N ABD AAC/AAT | | NOI | | | AWC/AWT | | | | | | | | | | |
| and | N K | and | SITI | | | N | | | | | | | | | | |
| Firet | AGG/AGA | First | NGLB PC | AKT/ | WGG/YGG | YGC/YGT | CRG/CRA | CRC/CRT | ARG/ARA | AKA/ | SGC/RGA | CSC/CST | ASA/ASG | CKG/CKC | MGC/MGT | |
| Code- | R Arg | Code- | A 9I | 2 | R. | 2 | S. | Z | ¥ | RI | 20 | RP | RT | 7. | 83 | |
| The Genetic Code- First and Second | GGC/GCT | Genetic Code- First and Second | BASES AT A SINGLE POSITION | GMC/GMT | GMG/GMP | GSC/GST | SCC/SCT | xcc/xct | RCC/RCT | GYC/GYT | | | | | | |
| The | Ala | The | TWO | 2 | 2 | 2 | AP | ş | AT | ¥ | | | | | | |
| | | | | | | | | | | | | | | | | |

FIGURE 13

Single letter code

Y = C or T

K = G or T

S = C or G

W = A or T

B = C or G or T

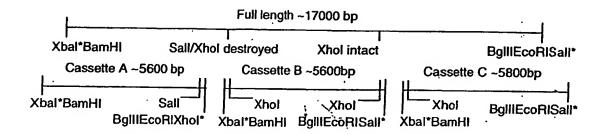
U = A or C or T

N = A or C or T

in many to the installant

| | crg/crc | | | 1/WTG | / TYA / GWA | (CAT | /MIT | CYC/CYG STG/STC |) CRC | | | 5 | 9/2 | 21 | 6 | | | | | |
|---|------------------|---|----------------------------|-------------------------------|----------------|--------------------|---------|--------------------|--------------------|--------------------|---------|-------|-------|----|---------|--------|--------|--------|--------|--|
| | 5 | | | MYG | 5 5 | 5 | E E | STG | 3 | | | | | | | | | | | |
| | r Fer | | | E A | ន្ទន | ' E ! | ää | និនិនិ | Ĭ | | | | | | | | | | | |
| | GTG/GTC | | | RTG/ GWC/GWT | KTC/KTT | RTC/RTT | GKG/GKC | srd/src | | | | | | | | | | | | |
| | v Val | Acids | | ₹9 | V V | I A | 9 | 3 | | | | | | | | | | | • | |
| | y Tyr tac/taf | More Amino Acids | | WAC/WAT KAC/KAT | YAC/YAT | TWC/TWT | | | | | | | | | | | | | | |
| | ۶ ۲ | More | | \$9 \$ | z Ķ | YF | } | | | | | | | | | | | | | |
| | 199/ | TWO or | | WGG/YGG KGG/ | TKG/ | TGS/TGK | | · | ٠ | | | | | | | | | | | |
| | ¥ Jžp | For | | X 25 2 | 2 2 | ខ្ល | | | | | | | | | | | | | | |
| | T Thr ACC/ACA | Frequently Used Degenerate Codons | | AYG/ AMC/AMT | AYC/AYT | RCC/RCT ASA/ASG | ASC/WCC | | | | | | | | | | | | | |
| ans | T Thr | nerat | | EEE | Ħ | e e | H. | | | | | | | | | | | | | |
| Frequently Used Codons | AGC/TCC | sed Dege | | TSG/ ARC/ART TYG/TYA | WGC/WGT | TYC/TYT | AKC/AKT | RGC/RGT YCC/YCT | ASC/WCC MGC/MGT | | | | | | | | | | | |
| ly u | Ser | ly u | | S SN | 2 | s y | 180 | 8 8 | ST | | | | | | | | | | | |
| Frequent | מככ/ככב | Frequent | | CMG/CMA CMC/CMT SCC/SCT | csc/csr | YCC/YCT | MCC/MCT | | | | | | | | | | | | | |
| | Pro | | | 2 2 2 | E 2 | 3 S | ፳ | | | | | | | | | | | | | |
| Second 1 | TTC/TT | Second 1 | NO | TKC/TKT WTC/WTT YTC/YTT | TYC/TYT | KTC/KTT | | | | | | | | | | | | | | |
| and | P | and | SITI | 5 I I | 82 83 | 2 2 | | | | | | | | | | | | | | |
| - First | ATG/ | - First | INGLE PO | AKT/ ATS/ATK MTG/WTG | AWG/ | RTG/ | | | | de | | | | | | | | | or T | |
| Code | Met Tet | Code | Ø | & # 4 | ¥ £ | ₹ | | | | 20 | | | | | or T | or T | or G | or T | or G | |
| The Genetic Code- First and Second Most | AAG/AAA | The Genetic Code- First and Second Most | BASES AT A SINGLE POSITION | ang/ aas/aam mag/maa | RAG/RAA | AMG/AMA | AWA | | | Single letter code | A or G | 0 0 C | 0 0 U | | or C | Corgo | | or G | | |
| The | r, x | The | TWO | £ § § | | | | | | Sing | H CX | > | 8 B | 3 | # | e M | n > | 8 A | o Z | |

FIGURE 13 (cont)



Full length construction after cloning the cassettes into pBS Sites marked with a *** are in the pBS MCS

Cassette Extras (Can be removed from cassette ends)

| A (37bp) BamHl/Kozak Start | Sall Stop Bglil EcoRl |
|---|--|
| 5' gc ggatccacc atg B (43bp) BamHI/Kozak Start Xhol | gtcgac tga agatct gaattc gc 3' Xhol Stop Bglll EcoRl |
| 5' gc ggatccacc atg ctcgag C (37bp) BamHI/Kozak Start Xhol | ctcgag tga agatgt gaattc gc 3' Stop Bglll EcoRl |
| 5' gc ggatccacc atg ctcgag | tga agatet gaatte ge 3' |

FIGURE 14

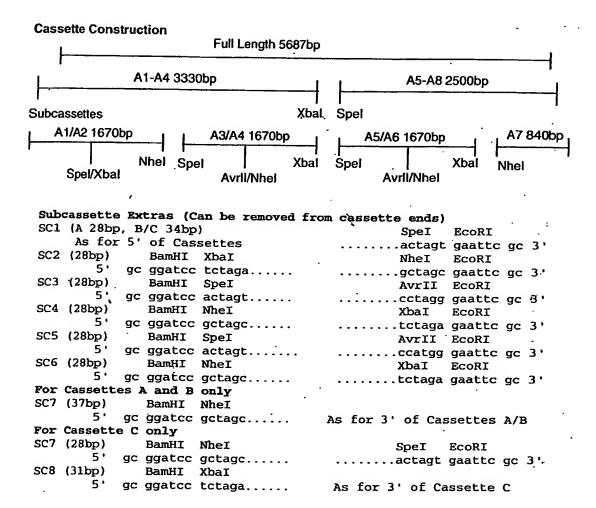


FIGURE 14 (Cont)

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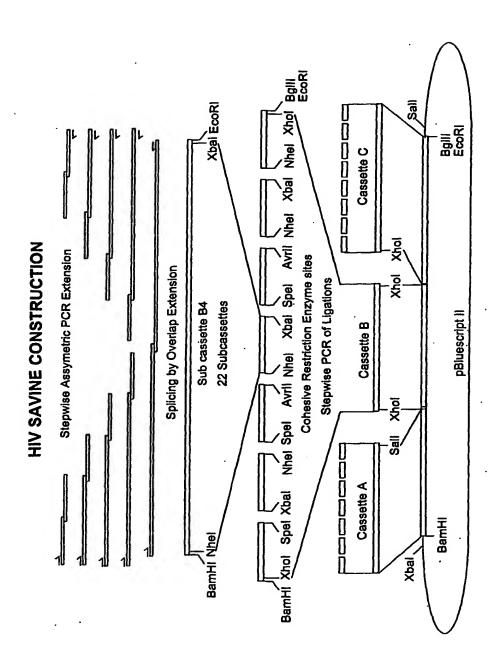


FIGURE 14 (Cont)

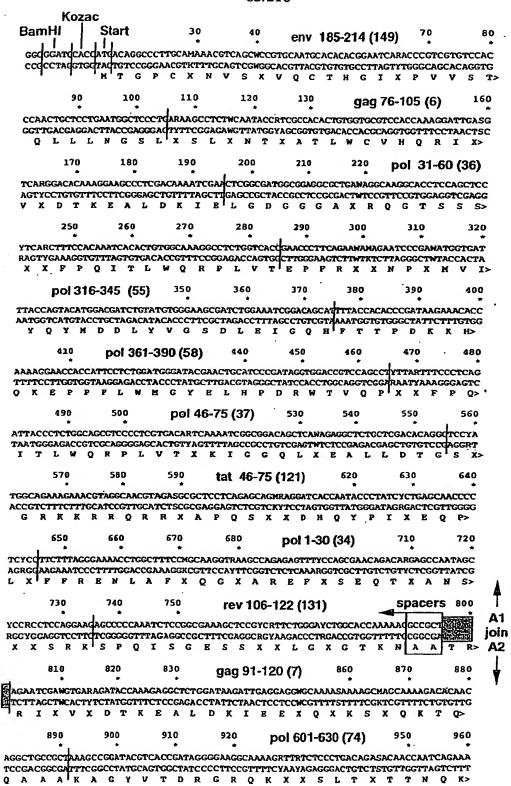


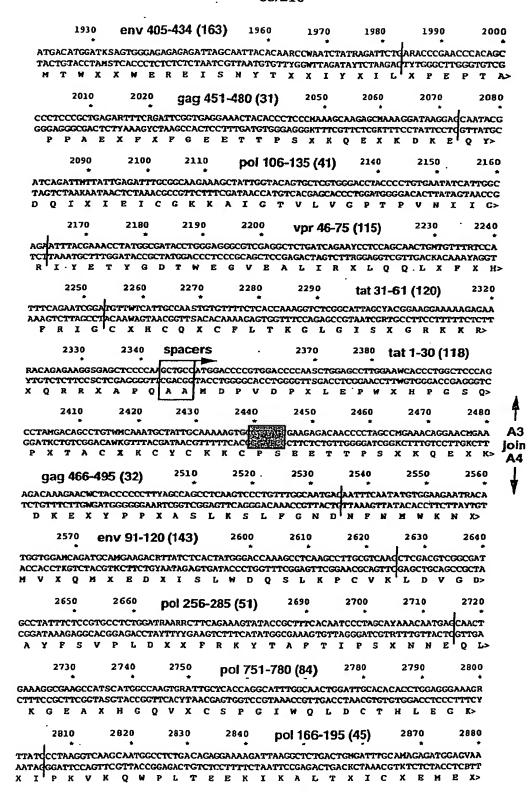
FIGURE 15

| 970 | 980 9 | 90 1000 | 1010 | env 46-75 | (140) 1040 | |
|--------------------------------------|--|-------------------------------------|-------------------|-------------------------------|---|-----|
| ACCGAACTGCAWGC | CATTCAMCAMCCCB | MTACCAC ACTCTT | PTYCCCCCACCCAT | YECCAAACCCVATY | ASACAGAGGTOCA | |
| TGGCTTGACGTWCG | • | • | | | | |
| T E L X A | | X T T L P | | | | |
| | | | | | | |
| 1050 | 1060 10 | 70 1080 | 1090 | pol 76-105 | (39) 1120 | |
| • | • | •, • | * | po. 70 .00 | . (00) | |
| CAATGTGTGGGCCA | CACACGCTTGCGTC | CCCCCTGACGATAC | CAGTGCTGGAGGA | SATSAACCTCCCC | GGAARATGGAAGC | |
| GTTACACACCCGGT | | | | | | |
| N'V W A | THACV | PADD1 | VLEX | XNLP | G X W K> | |
| | | | | | | |
| 1130 | 1140 119 | 1160 | 1170 | 1180 1 | 190 1200 | |
| CTAAGATGATTGGCC | ************************************** | والمحمدة والمحددة | PC140000100000 | | TA COCCA DITIONS | |
| GATTCTACTAACCGC | | | | | | |
| | G I G G P | | | | | |
| , , , , | G I G G I | 1 " 1 " | | | | |
| pol 196-22! | 5 (47) 123 | 0 1240 | 1250 | 1260 13 | 270 1280 | |
| poi 130-22. | (47) | • | • • | • | • | |
| GCTATCAAGAAAAAG | | | | | | |
| CGATAGTTCTTTTTC | | | | | | |
| · A I K K K | D S T K W | RKLV | DPRIX | RIIXI | L Y Q S> | |
| | 40 45 4455 | | 1220 | 1740 17 | 50 1360 | |
| 1290 I | rev 16-45 (125 |) 1320 | 1330 | 1340 13 | 50 1360 | |
| CAATCCCTATCCTAG | ביירונים מכוכושרוים | - | EA ATACCIACIA ACC | ACATERICEAGEC | AACRGGRTAGGG | |
| CTTAGGGATAGGATC | | | | | | |
| | SEGXI | | | | | |
| | | • • | | | | |
| 1370 | 1380 env 5 | 25-554 (171) | 1410 | 1420 14 | 30 1440 | |
| * | • | | • | • | *************************************** | |
| ATAGGTCCGTGAGAC | | | | | | |
| TATCCAGGCACTCTG | CCAGFIGCCIAAGA . V X G F | | | | | |
| DRSVRI | , v x G F | | <i>U U U</i> K | X L C L | , , to 10- | |
| 1450 | 1460 1470 | env 31⊣ | SO (120) | 1500 15: | 10 1520 | |
| • | * * * | CITY 317 | 00 (109) | • | • | |
| TGGGTCACCGTCTACT | | | | | | |
| ACCCAGTGGCAGATGA | | | | | | |
| WVTVY | ACABA | WRXA | XTTLF | CASD | A K A X> | |
| spacers | 1550 | 1560 | 4.00 44 | 24) 159 | 0 1600 | |
| Spacers | 1350 | * | rev 1-30 (1 | 24) | | |
| dectecoatesctesc | AGAAGCGGCRRCAC | AGACGAAGAGCTC | TGARGGCTRTCA | GAATCATTAASAT | TCTGTATCAGT | |
| CCACGCTACCGACCG | | | | | | |
| | R S G X T | | | | | A |
| | | | | | | 4 |
| 1610 | 1620 1630 | 1640 | 1650 | vif 16-45 (10 | 1) 1680 | 1 |
| * | | * | * | | memera a ca a a | A2 |
| CCAACCCTTACCCTTC GGTTGGGAATGGGAAG | | | | | | oin |
| | A S M X] | | | | | A3 |
| 5 N P I F 5 | A S H A J | | 2 L V K | | | A3 |
| 1690 | 700 1710 | 1720 | 1730 | 1740 175 | 0 1760 | 1 |
| * | * * | . * | * | * | • | V |
| GCCAAWGGCTGGTTCTA | TAGGCATCACTWTC | ASCACTCCCAGST | CGTGARTCAGATT | PATCGAAVAGCTC | ATCAAAAAGGA | • |
| CGGTTWCCGACCAAGAT | | | | | | |
| AXGWFY | | | | | | |
| | | • | | | | |
| pol 661-690 (7 | 78) ¹⁷⁹⁰ | 1800 | 1810 | 820 183 | 0 1840 | |
| • | • | * 1 | • | • | • | |
| AARGGTCTACCTAKCAT | | | | | | |
| TTYCCAGATGGAT#GTA | | | | | | |
| X V Y L X | WVPAH | KGIGI | QTKEL | . Q х Q І | X K I> | • |
| | | | | | | |
| | | | | | | |
| ¹⁸⁵⁰ pc | ol 916-945 (95) | 1880 | 1890 1 | 900 191 | 1920 | |
| • | | • | • | • | • | |
| AAAACTTTAGGGTCTAC | TATAGGGATAGCAG | * AGACCCTMTCTGG | ANGGGACCG AAAA | GCYTTGAGGAAA' | * CTGGRACAAT | |
| • | TATAGGGATAGCAG ATATCCCTATCGTC | * AGACCCTMTCTGG PCTGGGAKAGACC | ANGGGACCGAAAA | GCYTTGAGGAAA' CGRAACTCCTTT | * *CTGGRACAAT AGACCYTGTTA | |

FIGURE 15 (Cont)

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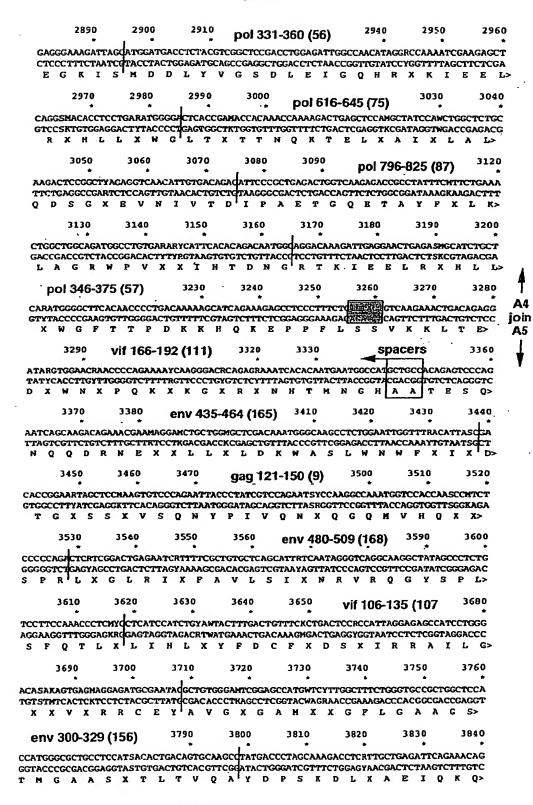
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FRGURE 15 (Cont)

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阿伊斯原 15 (Cont) SUBSTITUTE SHEET (RULE 26)

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A6

3870 pol 466-495 (65) 3880 3890 3900 3910 3920 GGTCAGGRTCAGTGGACATWTCAGATTTWCCAAGAGCCTTTCAAAAAAGGAACCGTCCTGGTCGGCCCTACACCCGTCAA CCAGTCCYAGTCACCTGTAWAGTCTAAAWGGTTCTCGGAAAGTTTTTCCCTTGGCAGGACCAGCCGGGATGTGGGCAGTT
G Q X Q W T X Q I X Q E P F K N G T V L V G P T P V N> 3960 3970 3980 3930 3990 4000 pol 121-150 (42) CATCATCGGAAGGAACHTGCTGACACAGHTTGGCYGCACCCTCAACTTTCCCATTAGGAAAGGCAGCCCTGCTATCTTTC GTAGTAGCCTTCCTTGKACGACTGTGTCKAACCGRCGTGGGADTTGAAAGGGTAATCCTTTCCGTCGGGACGATAGAAAG I I G R N K L T Q X G X T L N P P I S K G S P A I P> 4010 4020 4050 4060 4070 4080 pol 301-330 (54) AGTCCAGCATGMCAMAGATTCTGGAGCCTTTTAGGAWAMAAAACCCTGASATGGTCATCTATCAGTAT CCTCTG tcaggtcgtackgtktctaagacctcggaaaatcctwikttitgggactstaccagtagatagtcatk Q S S M X X I L E P F R X X N P X M V I Y Q Y 4150 4110 4100 nef 136-165 (188) 4140 4160 ACATTCGGATGGTGTTTCAAACTGGTCCCCGTGGACCCCAGSGAAGTGGAAGAGRYCAACRAGGGCGAAAACAATTGCCT TGTAAGCCTACCACAAAGTTTGACCAGGGGCACCTGGGGTCSCTTCACCTTCTCYRGTTGYTCCCGCTTTTGTTAACGGA GWCPKLVP V D P X E V E E X N X G E N N C L> 4170 4180 4190 4200 4230 4240 pol 271-300 (52) ${\tt CCT} {\tt TTTAGGAAATACACACCTTTACCATTCCCAYCAATAACGAAACCCCTGGCATTAGGTATCAGTATAACGTCC}$ GGAÇAAATCCTTTATGTGTGGGAAATGGTAAGGGAGGTRGTTATTGCTTTGGGGACCGTAATCCATAGTCATATTGCAGG PRKYTAFTIPSXNNETPGIRYQYNV> 4270 4280 4290 4260 env 315-344 (157) 4250 TGCCTCAGGGATGGGAAGCACAATGGGAGCCGCCAGCATKACCCTCACCGTCCAGGCTAGGCWACTGCTCAGCGGAATC ACGGAGTCCCTACCCTTCGTGTTACCCTCGGCGGTCGTAMTGGGAGTGCCAGGTCCGATCCGWTGACGAGTCGCCTTAG L P Q G W G S T M G A A S X T L T V Q A R X L L S G I> 4370 pol 451-480 (64) 4340 4350 4360 GTCCAGCAACAGARCAATCTGCT4GHGGAGAATAGGGAAATCCTCARAGAGCCTGTGCATGGGGTCTACTACGATCCCTC CAGGTCGTTGTCTYGTTAGACGACKCCTCTTATCCCTTTAGGAGTYTCTCGGACACGTACCGCAGATGATGCTAGGGAG V Q Q Q X N L L X E N R E I L X E P V H C V Y Y D P S 4420 4430 4440 4450 vpu 61-81 (136) GTTCCTAGACYAGCGACTTYAGGTTTTCGTTCCGTSTCTCCTTGACAGGYGGNACCACCTATACCCTTTGATGCTGGAGC

K D L X A B X Q K Q G X E E L S X X V D H G N Y D L> spacers 4560 4510 4520 4530 vpr 61-90 (116) GAGTGGACAATAACCTGGCCGCTATTAGAAYCCTGCAACAGCTCMTGTTCRTTCACTTTAGGATTGGCTGCCRGCACTCC CTCACCTGTTATTGGACGGCGGTAATCTTRGGACGTTGTCGAGKACAAGYAAGTGAAATCCTAACCGACGGYCGTGAGG G V D N N L A A I R X L Q Q L X P X H P R I G C X H S> gag 406-435 (28) 4640 4590 4600 4610 aggattggcatchyccgtcagagaagggscag/gctccaggaaaaagggatgctggaagtgtcgcaragagggcacca TCCTAACCGTAGKRGGCAGTCTCTTCCCSGTCCGAGGGTCCTTTTTCCCTACGACCTTCACACCGTYTCTCCCTGTGGT
R I G I X R Q R R X R A P R K K G C W K C G X E G H O APRKKGCWKCGXBGHQ> 4700 4650 4660 4670 4680 4690 GATGAAGGATTGCACTGAGAGACAGGCTAACTTTCTGGGAAAGGAWGCCAGACTGRTTATCARAACCTATTGGGGACTGC CTACTTCCTAACGTGACTCTGTCCGATTGAAAGACCCTTTCCTWCGGTCTGACYAATAGTYTTGGATAACCCCTGACG
M K D C T E R Q A N P L G K X A R L X I X T Y W G L> . 4780 4790 4800 4750 4760 4770 vif 61-90 (104) ATACCGGTGAGAGAGACTGGCASCTCGGCCAWGGCGTCAGCATTGAGTGGAGGAYAAGGGAAAGGGCTGAGGATAGCGGC TATGGCCACTCTCTGACCGTSGAGCCGGTWCCGCAGTCGTAACTCACCTCTTTTCCCGTTTCCCGACTCCTATCGCCG
H T G E R D W X L G X G V S I E W R X R E R A E D S G>

FIGURE 15 (Cont)

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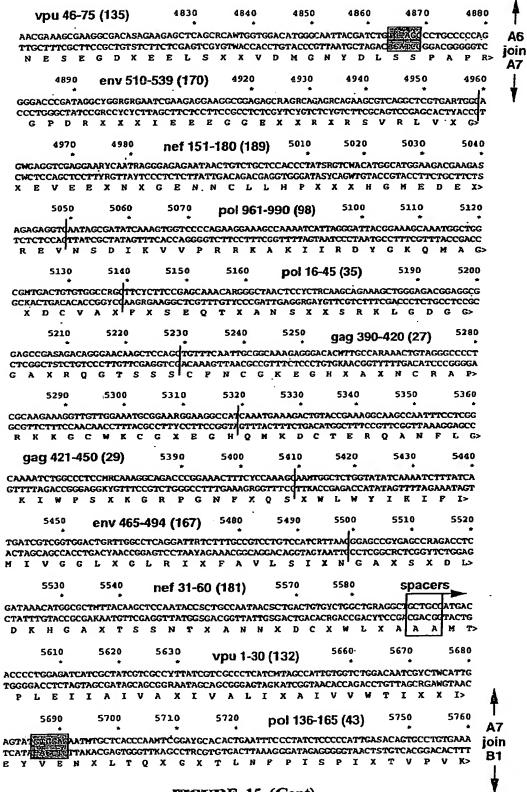


FIGURE 15 (Cont)
SUBSTITUTE SHEET (RULE 26)

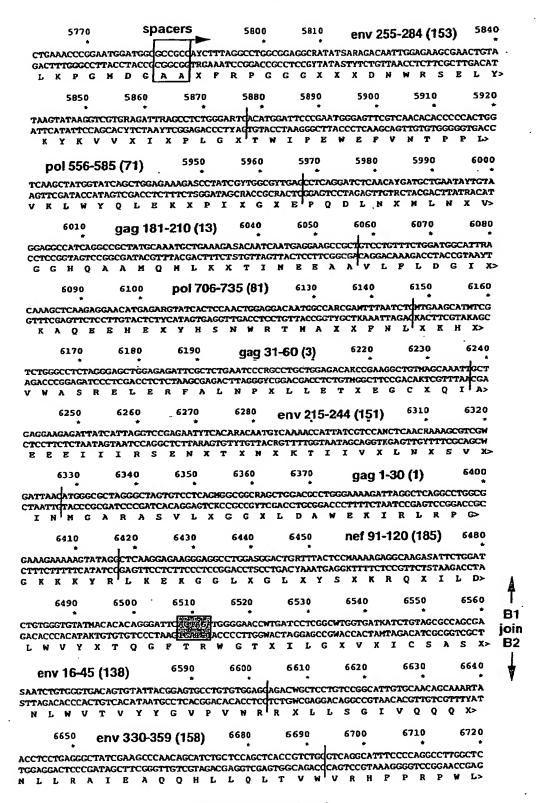
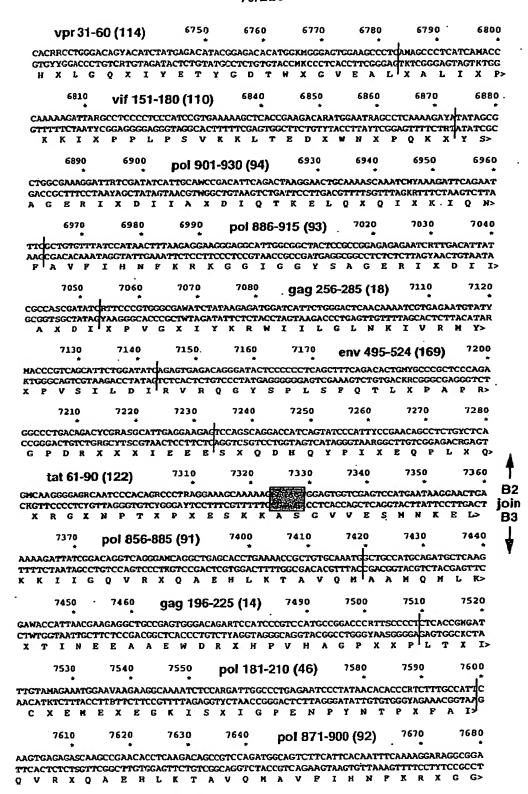


FIGURE 15 (Cont)

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REGURE 15 (Cont)

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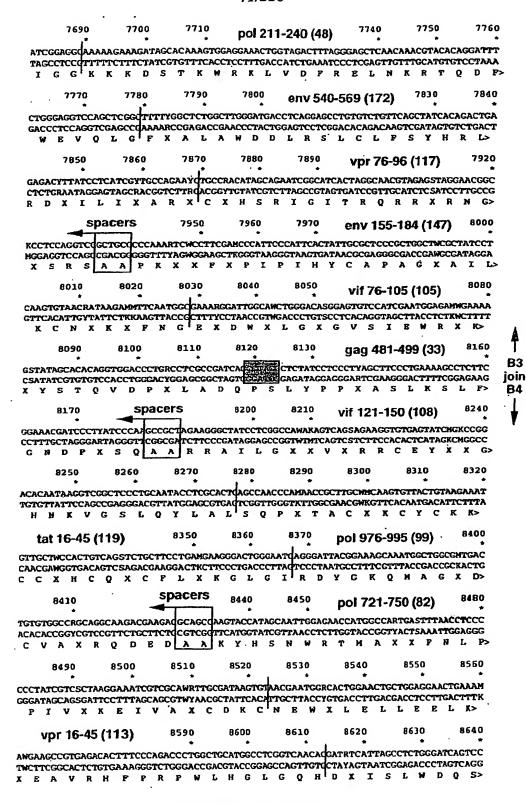


FIGURE 15 (Cont)
SUBSTITUTE SHEET (RULE 26)

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9590

ASYCGGWTGTGCCTTACCTCCTACTCCTWTCCCTTCACGACTWTACCTTTAAGCTATCGGYAGACCGAGHGTCCGTATAS XXX H G N E D E X R E V L X W K P D S X L A X R H X> 8910 8920 pol 151-180 (44) 8960 GCT RESTREE CCTATCGAWACCGTCCCCGTCAAGCTCAAGCCTGGCATGGACGGACCCAAAGTGAAACAGTGGCCCCCTCAC

GGATAGCTWTGGCAGGGGCAGTTCGAGTTCGGACCGTACCTGCCTGGGTTTCACTTTGTCACCGGGGAGTG PIXTVPVKLKPGMDGPKVKQWP 8970 8980 8990 9000 9010 gag 436-465 (30) 9040

TSRGCCWACACGGAATGGAGGATGAGGAWAGGGAAGTGCTGAWATGGAAATTCGATAGCCRTCTGGCTCKCAGGCATATS

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CTGAAACCCTGTGTGAAACTGACACCCCTCTGCGTCACCCTCAACTGTACCAATGCCAATCTQHKGAAGAGHTACTCCAC GACTTTGGGACACACTTTGACTGTGGGAGACGCAGTGGGAGTTGACATGGTTACGGTTAGACAWCTTCTCKATGAGGTG L K P C V K L T P L C V T L N C T N A N L X K X Y S T>

8690

8700

8780

8680

vif 91-120 (106)

8830

env 106-144 (144)

8740

8820

8900

8730

8810

9530

9540

9550

CGAAGAGAAAATCAAAGCQATTTGGCCTAGCMRCAAGGGAAGGCCTGGCAATTTCCYGCAGTCCARGCCTGAGCCTACCG GCTTCTCTTTTAGTTTCGGTAAACCGGATCGKYGTTCCCTTCCGGACCGTTAAAGGRCGTCAGGTYCGGACTCGGATGGC EEKIKAIWPSXKGRPGNPXQSXPEPT>

9050 9060 9070 9090 vif 31-60 (102) 9120 CACCCCCAGCCGAGARCTTTRGATTCGGCATTAGCAAAAAGGCTAASGGATGGTTTTACAGACACCATTWCGAWAGCCRAGGGGGGTCGGCTCTYGAAAYCTAAGCCGTAATCGTTTTTCCGATTSCCTAACAAAATGTCTGGGTAAWGCTWTCGGYT PPAEXPXFGISKKAXGWPYRHHXXSX>

9130 9140 9150 9160 9170 9180

gag 346-375 (24) 9230 9240 9250 9260

AGCCAGGGTACTGGCAGAGGCTATGTCCCAGGYGAMCHACGCTAACATTCCTCCCATTGTGSCCAAAGAGATTGTGGCAM TCGGTCCCATGACCGTCTCCGATACAGGGTCCRCTKGKTGCGATTGTAFGGAGGGTAACACSGGTTTCTCTAACACCGTM A R V L A E A M S Q X X X A N I P P I V X K E I V A> 9290 pol 736-765 (83) 9320 9330 9340 9350 9360

 ${\tt RCTGTGACAAATGCCAGCTCAAGGGTGAGGCTATKCACGGACAGGTGRACTGTAGCCCTTCCGAGGGAWCAAGACAGRCT}$ YGACACTGTTTACGGTCGAGTTCCCACTCCGATANGTGCCTGTCCACYTGACATCGGGAGGCTCCCTMGTTCTGTCYGA X C D K C Q L K G E A X H G Q V X C S P S E G X R Q X>

9370 9380 rev 31-60 (126) 9410 9420 AGGARGAACAGACGTAGAAGGTGGCGTGMGAGGCAAAGGCAAATCCRCKCCATCTCCGAGWGGATTCTGGGACAGATRAG TCCTYCTTGTCTGCATCTTCCACCGCACKCTCCGTTTCCGTTTAGGYGHGGTAGAGGCTCWCCTAAGACCTGTCTAYTC R X N R R R R R R R R R Q R Q I X X I S E X I L G Q X R>

9450 9460 9470 9510 9500 gag 226-255 (16) GGAACCCAGAGGCTCCGACATTGCCGGTACCACAAGCACACTGCAAGAGCAAATCGSATGGATGACAARCAATCCCCC¶R

CCTTGGGTCTCCGAGGCTGTAACGGCCATGGTGTTCGTGTGACGTTCTCGTTTAGCSTACCTACTGTTYGTTAGGGGGA EPRGSDIAGTTSTLQEQIXWMTXNP

9560

pol 841-870 (90) RCATTMAGCAAGAGTTTGGCATTCCCTATAACCCTCAGTCCCAGGGCGTCGTGGAAAGCATGAACAAAGAGCTCAAGAAA YGTAAKTCGTTCTCAAACCGTAAGGGATATTGGGAGTCAGGGTCCCGCAGCACCTTTCGTACTTGTTTCTCGAGTTCTTT XIX Q E F G I P Y N P Q S Q G V V E S M N K E L K K>

FIGURE 15 (Cont)

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B4 join **B5**

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B5

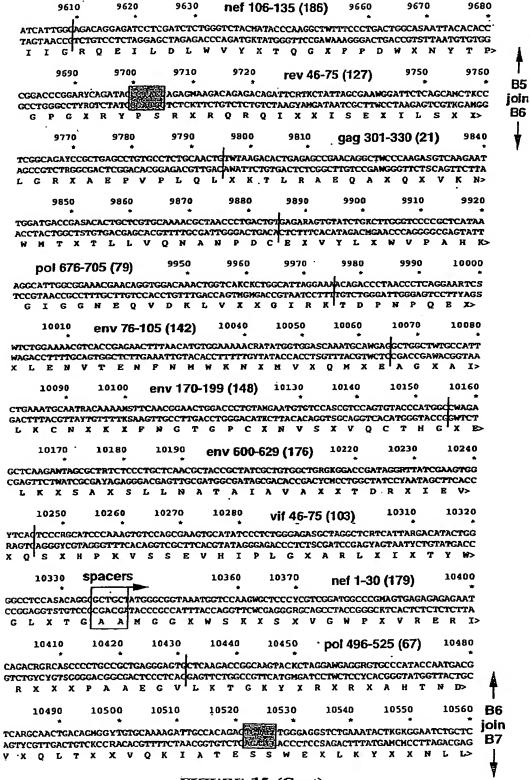


FIGURE 15 (Cont)

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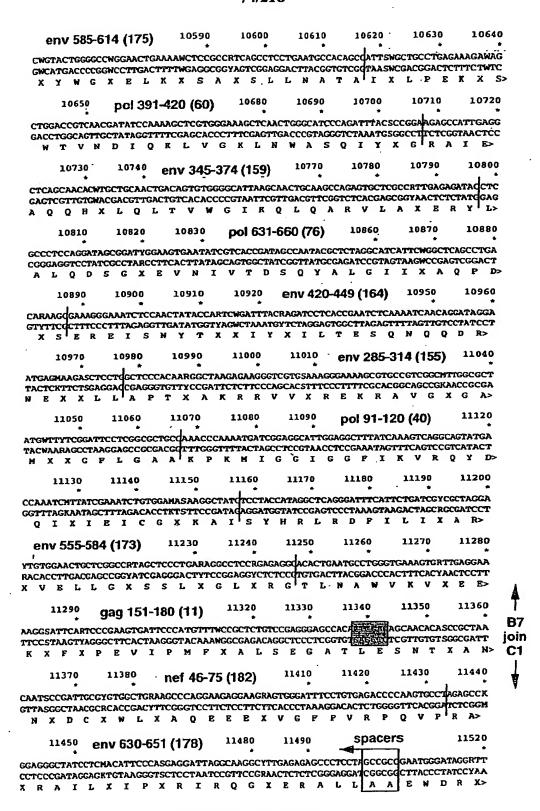


FIGURE 15 (Cont)

```
11600
                                                                  11590
                                                        11580
                                              11570
                        gag 211-240 (15)
               11540
     11530
CACCCTGTGCACGCTGGCCCTRTCSCTCCCGGCCAAATSAGAGAGCCCAGGGGAAGCGATATCGCTGGCACAACCCTCAG
GTGGGACACGTGCGACCGGGAYAGSGAGGGCCGGTTTASTCTCTCGGGTCCCCTTCGCTATAGCGACCGTGTTGCGAGTC
 HPVHAGPXXPGQXREPRGSDIAGTTLR>
                                                                            11680
                                                                  11670
                                                        11660
                       11630
                                   nef 76-105 (184)
               11620
     11610.
GCCCATGACATATAAGGSCGCTRTTGACCTCAGCYTGTTTCTGAAAGAGAAAGGCGGACTGGAWGGCCTCRTCTATAGCM
CGGGTACTGTATATTCCSGCGAYAACTGGAGTCGRACAAAGACTTTCTCTTTCCGCCTCACCTWCCGGAGYAGATATCGK
  PHTYKXAX DLS L PLKEKGGLXGLXY 5>
                                                                  11750
                                    11720
                                               vpr 1-30 (112)
                         11710
AGAAAGCTGCTATGGAACAGCTCCCGAAGACCAARGCYCTCAGAGAGAGCCTTACAATGAGTGGRCCCTGGAGCTCCTG
    spacers
TCTT CGACGATACCTTGTCCGAGGGCTTCTGGTTYCGRGAGTCTCTCTCGGAATGTTACTCACCYGGGACCTCGAGGAC
X K A A M E Q A P E D Q X X Q R E P Y N E W X L E L L>
                                                        poi 481-510 (66)
                                              11810
                         11790
                                    11800
               11780
     11770
GAAGAGCTCAAGHAHGAGGCTCAAGRCCAATGGACCTWCCAAATCTWTCAGGAACCCTTTAAGAATCTGAAAACCGGAAA
CTTCTCGAGTTCKTKCTCCGAGTTCYGGTTACCTGGAWGGTTTAGAWAGTCCTTCGGAAATTCTTAGACTTTTGGCCTTT
E E L K X E A Q X Q W T X Q I X Q E P F K N L K T G K>
                                                                            11920
                                                                  11910
                                                        11900
                                              11890
                                    11880
                          11870
               11860
     11850
GTATKCCAGAAWGAGARGCGCTCACACAAACTGGATGACAGAWACCCTCCTGGTCCAGAATGCCAATCCCGATTGCAAGW
CATAMGGTCTTWCTCTYCGCGAGTGTGTTTCACCTACTGCTTWTGGGAGGACCAGGTCTTACGGTTAGGGCTAACGTTCW
Y X R X R X A H T N W H T X T L L V Q N A N P D C K>
                                                                             12000
                                              11970
                                                        11980
                                    11960
                         11950
  gag 316-345 (22)
CCATCCTCARGGCTCTGGGAHCCGGAGCCWCACTGGAAGACCCTGAGGTCATCCCTATGTTCWCAGCCCTCAGCGAAGGCGCTGGGAGGTTCCCGAGGAGTTCCGGAGCTCCAGGAGCCCTKGGCCTCGGHGTGACCTTCTGGGACTCCAGTAGGGATACAAGMGTCGGGAGTCGCTTCCGXX I L X A L G X G A X L E E P E V I P M P X A L S E G>
                                                                  12070
                                                        12060
                                              12050
                                    12040
              gag 166-195 (12)
     12010
12150
                                                        12140
                         gag 241-270 (17)
                                              12130
               12100
GACAARTAACCCTCCCRTCCCTGTCGGAGASATTTACAAAAGGTGGATTATCCTCGGCCTGAATACCCCCATCCCG

JOIN
CTGTTYATTGGGAGGGYAGGGACAGCCTCTSTAAATGTTTCCACCTAATAGGAGCCGGAGGATTATCCTCGGCCTG
      12090
  TXNPPXPVGXIYKRWIILGLT
                                                                             12240
                                                        12220
                                   pol 241-270 (50)
                          12190
                12180
      12170
CCGGCCTCAAGAAAAAGAAAAGCGTCACCGTCCTGGATGTGGGAGACGCTTACTTCAGCGTCCCCCTCGACRAARRQCAA
GGCCGGAGTTCTTTTCTTTTCGCAGTGGCAGGACCTACACCCTCTGCGAATGAAGTCGCAGGGGGAGCTGYTTYY
A G L K K K S V T V L D V G D A Y F S V P L D X X
                                                                             12320
                                                                  12310
                                              pol 541-570 (70)
                                    12280
                          12270
                12260
      12250
ARGGAAACCTGGGAGRCTTGGTGGAYGGAMTACTGGCAGGCTACCTGGATTCCTGAGTGGGAGTTTGTGAATACCCCTCC
TYCCTTTGGACCCTCYGAACCACCTRCCTKATGACCGTCCGATGGACCTAAGGACTCACCCTCAAACACTTATGGGGAGG
 X E T W E X W W X X Y W Q A T W I P E W E F V N T P P>
                                                       nef 121-150 (187)
                                               12370
                          12350
                                    12360
                12340
      12330
 CCTCGTCTTTCCCGATTGGCAMAACTATACCCCTGGCCCTGGCRYAAGGTATCCCCTCACCTTTGGATGGTGCTTTAAGC
 GGAGCAQAAAGGGCTAACCGTWTTGATATGGGGACCGGGACCGYRTTCCATAGGGGAGTGGAAACCTACCACGAAATTCG
   L V F P D W X N Y T P G P G X R Y P L T P G W C F K>
                                                                             12480
                                                        pol 571-600 (72)
                                               12450
                                     12440
                          12430
                12420
 TCGTGCCTGTGGACCCQAAACTGTGGTACCAACTGGAAAAGGAMCCCATTGYCGGAGYCGAAACCTTTTACGTGGACGGA
AGCACGGACACCTGGGGTTTGACACCATGGTTGACCTTTTCCTXGGGTAACRGCCTCRGCTTTGGAAAATGCACCTGCCT
L. V P V D P K L W Y Q L E K X P I X G X E T F Y V D G>
```

FIGURE 15 (Cont)

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12500 12490 12510 12520 gag 136-165 (10) GCCGCCARCAGAGAGACAAAGCTCGGGCAAAAACSYCCAGGGACAGATGGTGCATCAGSCTMTTAGCCCCAGGACCCTCAA CGGCGGTYGTCTCTCTGTTTCGAGCCGGTTTTGSRGGTCCCTGTCTACCACGTAGTCSGAKAATCGGGGTCCTGGGAGTT AAXRETKLGQNXQGQMVHQXXSPRTLN> 12570 12580 12590 12600 ¹²⁶¹⁰ env 61-90 (141) 12640 ${\tt cgcttgggtcaaggtcaaggagaaggsctttar} \\ {\tt dgaagccgaagtgcataacgttgggctacccatgcctgtgc} \\$ GCGAACCCAGTTCCAGYAGCTTCTCTTTCSGAAATYGCTRTGGCTTCACGTATTGCAGACCCGATGGGTACGGACACACG
A W V K V X E B K X F X X T E V H N V W A T H A C V> 12650 12670 12680 12690 12700 12710 12720 CTACCGATCCCAATCCCCAAGAGRITSWCCTGGAGAATGTGACAGAGCTCAAGGATCACHAAYTCCTCGGCHTTTGGGGA GATGGCTAGGGTTAGGGGTTCTCYAASWGGACCTCTTACACTGTCTTGGAGTTCCTAGTCKTTRAGGAGCCGKAAACCCCT T D P N P Q E X X L E N V T E L K D Q X X L G X W G> 12750 12760 12770 env 375-404 (161) 12780 12790 12800 TGCTCCGGCAAAHTCATTTGCACAACCRMTGTGCCTTGGAACAGCWCCTGGTCCAACCMAKCTGGCCATAACAAAGTGGG ACGAGGCCGTTTKAGTAAACGTGTTGGYKACACGGAACCTTGTCGWGGACCAGGTTGGKTMGACCGGTATTGTTTCACCC C S G K X I C T T X V P W N S X W S N X X G H N K V G> vif 136-165 (109) 12840 12850 12860 12870 12880 AAGCCTCCAGTATCTGGCTCTGAMGGCTCTGATTAMGCCTAAGAAAATCARACCCCCTCTGCCTAGGGYTAAGACAATCA ttcggaggtcatagaccgagactkccgagactaatkcggattcttttagtytgggggagacggatcdcrattctgttagt S L Q Y L A L X A L I X P K K I X P P L P S X K T I> spacers 12890 12900 env 230-254 (152) 12930 12960 TTGTGCATCTGAATRAGTCCGTGGWAATCAATTGCACAAGGCCTARCAATAACACAAGGAMAGCCGCC cancua. AACACGTAGACTTAYTCAGGCACCWTTAGTTAACGTGTTCCGGATYGTTATTGTGTTCCTKCGGCGG V H L N X S V X I N C T R P X N N T R X A A A S E X> 12970 12990 gag 106-135 (8) 13020 13030 13040 CAGANWAAGTCCMAACAGAAAAACCCAGCAAGCCGCCGATACAGGCARCTCCAGCMAGGTCAGCCAAAACTATCCCAT GTCTTWTTCAGGKTTGTCTTTTGGGTCGTTCGGCCGCCGCTATGTCCGTTGAGGGTCGKTCCAGTCGGTTTTGATAGGGTA Q X K S X Q K T Q Q A A A D T G X S S X V S Q N Y P I> 13050 13060 13070 13080 pol 826-855 (89) TGT-TCCAACTTTACCTCCRCCRCTGTGAAAGCCGCTTGTTGGTGGGCCRRTATCMAACAGGAGTTTGGAATCCCTTACA AGGTTGAAATGGAGGYGGYGACACTTTCGGCGAACAACCACCCGGYYATAGKTTGTCCTCAAACCTTAGGGAATGT V S N P T S X X V K A A C W W A X I X Q B P G I P Y> 13140 13130 13150 13160 13170 pol 586-615 (73) ATCCCCAAAGCCAAACATTCTATGTGGATGGCGCTGCCARTAGGGAAACCAAACTGGGAAAGGCTGGCTATGTGACAGAC TAGGGGTTTCGGTTTGTAAGATACACCTACCGCGACGGTYATCCCTTTGGTTTGACCCCTTTCCGACCGATACACTGTCTG N P Q S Q^IT P Y V D G A A X R E T K L G K A G Y V T D> 13210 13220 13230 13250 13240 pol 766-795 (85) AGAGGCAGACAGAAARTCRTTAGGGGAATCTGGCAGCTCGACTGTACCCATCTGGAAGGCAAARTCATTCTGGTAGCCGT TCTCCGTCTGTCTTYAGYAATCCCCTTAGACCGTCGAGCTGACATGGGTAGACCTTCCGTTTYAGTAAGACCATCGGCA R G R Q K X X S G I W Q L D C T H L B G K X I L V A V> 13310 13320 13330 13340 13350 CCACGTCGCCTCCGCTACATTGAGGCTGAGGTGGCAATGAGCAAGTGGATAAGCTCGTGAKTKCCGGAATCAGAAAGG GGTGCAGCGGAGGCCGATGTAACTCCGACTCCAGCCGTTACTCGTTCACCCTTATTCGAGCACTMAMGGCCTTAGTCTTTCC
H V A S G Y I E A E V G N E Q V D K L V X X G I R X> pol 691-720 (80) 13390 13400 13410 13420

C3

FIGURE 15 (Cont) **SUBSTITUTE SHEET (RULE 26)**

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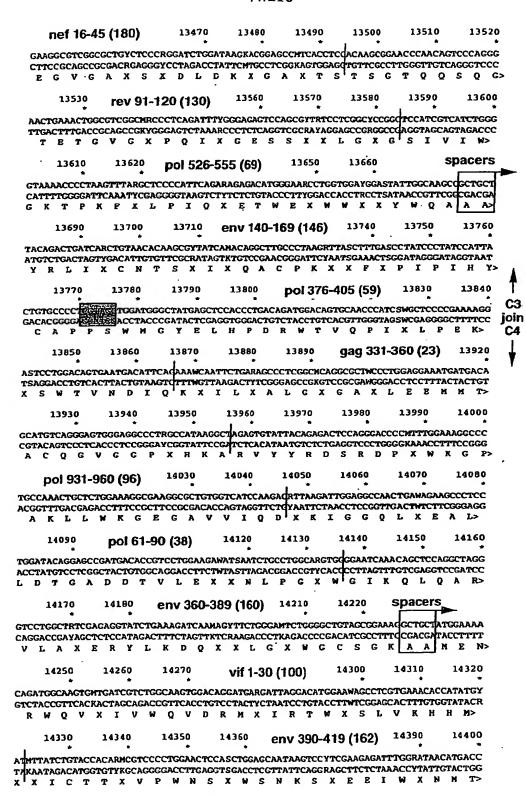


FIGURE 15 (Cont)

C4 join

C5

14410 14430 14420 vpu 16-45 (133) 14460 14470 14480 TGGATKSAATGQCTGATTHTCGCTATCGTCGTCTGGACCATTGYGTWTATCGAATACARGAAACTGCTCARGCAAAGGAR ACCTAMSTTACCGACTAAKAGCGATAGCAGCACCCTGGTAACRCAWATAGCTTATGTYCTTTGACGAGTYCGTTTCCTY W X X W L I X A I V V W T I X X I E Y X K L L X Q R X> 14490 14510 14520 gag 46-75 (4) 14550 AATCGATAGGCTCATCRAAAGGCTCAACCCTGGCCTCCTGGAAACCKCTGAGGGATGTHAACAGATCCTGGRACAGCTCC TTAGCTATCCGAGTAGYTTTCGGACTGGGACCGGAGGACCTTTGGAGACTCCCTACAKTTGTCTAGGACCYTGTCGAGG

1 D R L I X R L N P G L L P T X E G C X Q I L X Q L> 14570 14580 14590 14600 14610 QXALXTGXEELS S R K L L X Q R X I D R L I X> vpu 31-60 (134) 14670 14680 14690 14700 14710 AGANYCAGAGAGAGCCGAAGACTCCGGCAATGAGTCCGAGGGAGAACACCCGGAATCAGATACCAATACAATGTGCT TETTRETCTCTCTCGCCTTCTGAGGCCGTTACTCAGGCTCCCTCTQTGTGGGCCTTAGTCTATGGTTATGTTACACGA R X R E R A E D S G N E S E G D T P G I R Y Q Y N V L> 14730 pol 286-315 (53) 14760 14770 . 14780 14790 14800 CCCCCAAGGCTGGAAGGGCTCCCCASCCATTTTCCAAAGCTCCATCHCCMAAATCCTCATGATGCAAAGGGGAAACTTTA GGGGGTTCCGACCTTCCCGAGGGTSGGTAAAAGGTTTCGAGGTACXGGRTTTAGGAGTACTACGTTTCCCCTTTGAAAT
PQGNKCSPXIFQSSNXXILNMQRGNF> gag 376-405 (26) 14850 14860 14870 RGGGACNGAAAAGGATTRTCAAGTGCTTCAACTGTGGAAAGGAAGGCCATNTCGCTARGAATTGCAGACCTCCCTGGAG YCCCTGRCTTTTCCTAAYAGTTCACGAAGTTGACACCTTTCCTTCCGGTARAGCGATYCTTAACGTCTGGAGGGACCTC
X G X K R I X K C P N C G K E G H X A X N C R P P L E> 14900 14890 14910 14940 rev 76-105 (129) agactghacctggattgctccgaggatwgcgreacctccggeaeacaaggeaaaggcaeagaacaggagtggga<mark>c</mark>t TCTGACKTGGACCTAACGAGGCTCCTAWCGCYGTGGAGGCCGTGTGTGTTTCGGTTCCGTGTCTCTCTCACCCT R L X L D C S E D X X T S G T Q Q S Q G T E T G V G | 14970 14980 14990 15000 poi 781-810 (86) CGTGGCTGTGCATGTGGCCAGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTM GCACCGACACGTACACCGGTCGCCTATATAGCTTCGGCTTCACTAGGGACGGCTTTGACCTGTCCTTTGGCGAATGAAAX AVHVASGYIEAEVIPAETGQETAYF> 15050 15060 15070 15080 15090 env 200-229 (150) TCCTCAAGATTARGCCTGTGGTCAGCACACGCTCCTCCTCAACGGTACCCTCGCTGAACAGGAARTCRTTATCAGAAGC AGGAGTTQTAATYCGGACACCAGTCGTGTGTCGGAGGACGACTTGCCATCGGAGCGACTTCTCCTTYAGYAATAGTCTTCG X L K^II X P V V S T Q L L N G S L A B B B X X I R S> 15130 15140 15150 15160 pol 406-435 (61) GAAAACYTTACCRATAAdAAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACSCTGGCATCAAAGTGARGCAACT CTTTTGRAATGGYTATTGTTTGACCAGCCGTTTGACTTAACCCGAAGGGTTTAGATGSGACCGTAGTTTCACTYCGTTGA ENXTXN^IKLVGKLNWASQIYXGIKVXQL> 15210 15220 15230 15240 15250 env 121-139 (145) GTGTAAGCTCCTGAGAGGCRCCAAAGCCCTCACCCCTCTGTGTGACACTGAATTGCACAAACGCTAACCTCATCAATG CACATTCGAGGACTCTCCGYGGTTTCGGGAGTGGGGAGACACACACTGTGACTTACGTGTTTCCGATTGCGAGTACTTAC
C K L L R G X K A L T P L C V T L N C T N A N L I N> spacers 15310 15320 15330 15360 tat 76-102 (123) TGANTGCTCCTCAAMCCAGAGGCGATAACCCTACCGRTCCCRAAGAGTCCAAGAARAGGTCGMGTCCAAGRCAGAGACA actt/cgacg/gitkggtctccgctattgggatggcyagggyttctcaggttcttytccagckcaggttcygtctctgt N A A Q X R G D N P T X P X E S K K X V X S K X E T>

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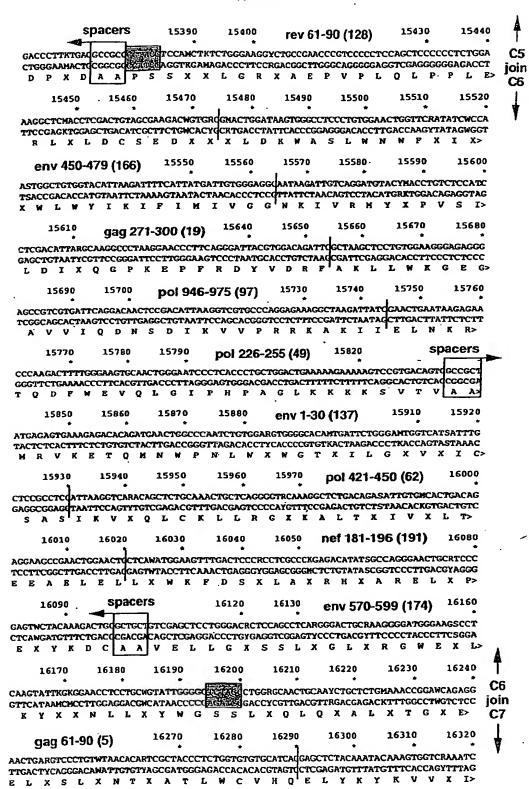


FIGURE 15 (Cont)

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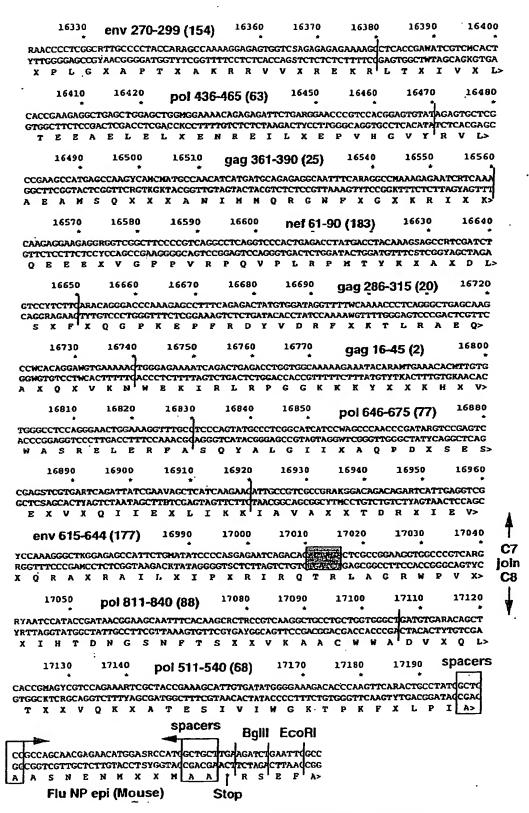
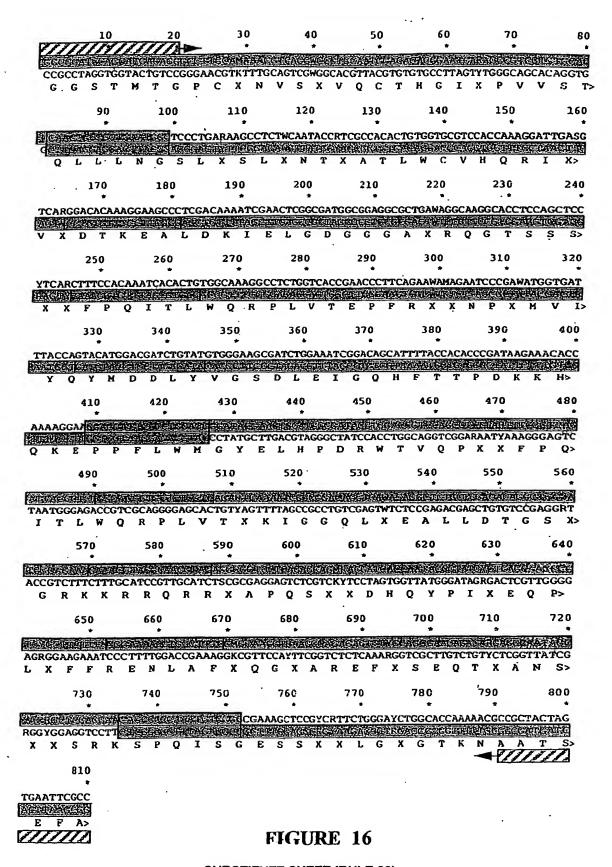


FIGURE 15 (Cont)



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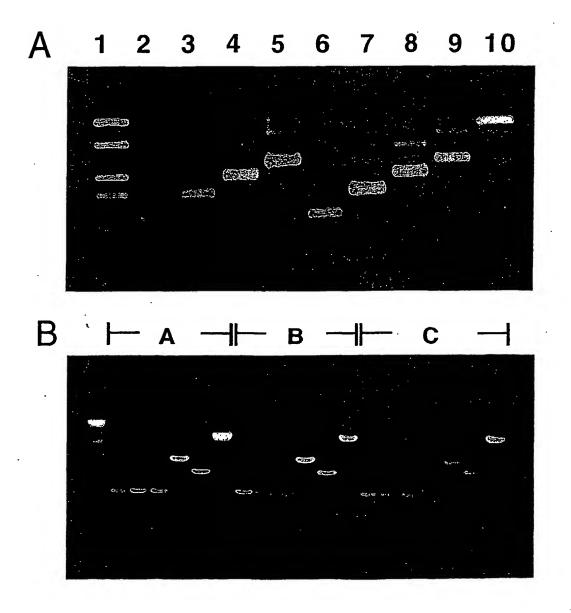


FIGURE 17

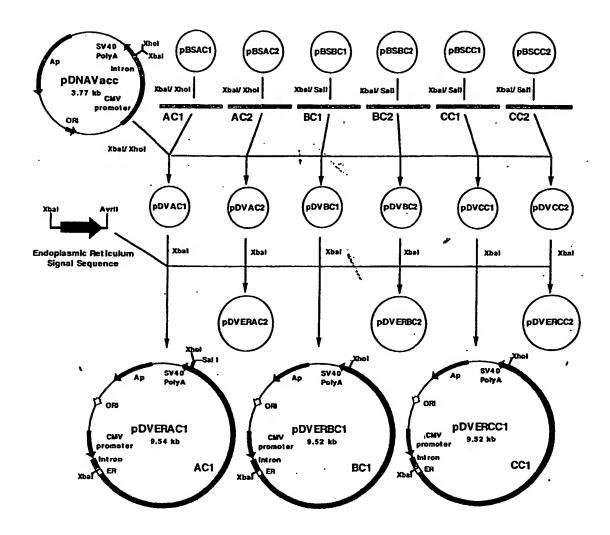


FIGURE 18A

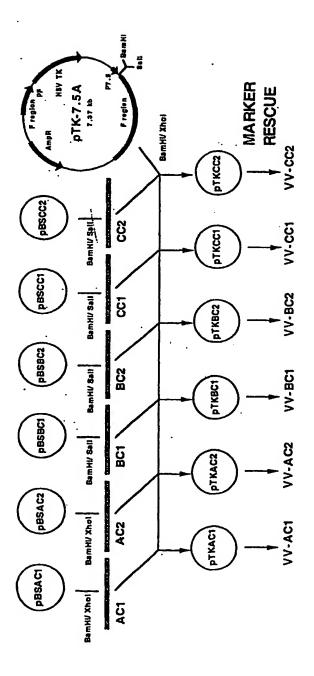


FIGURE 18B

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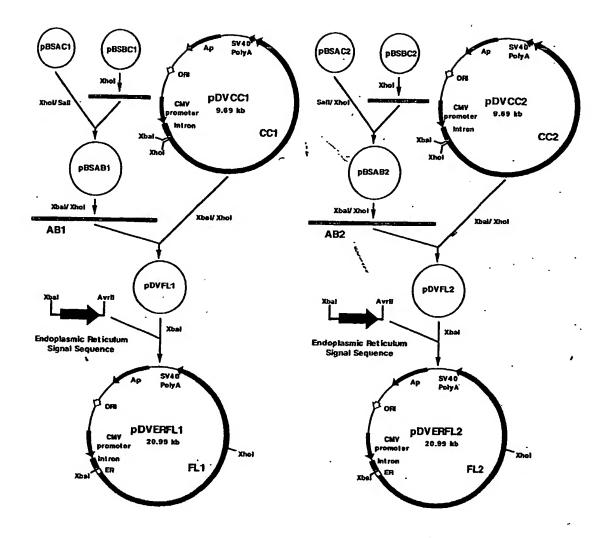
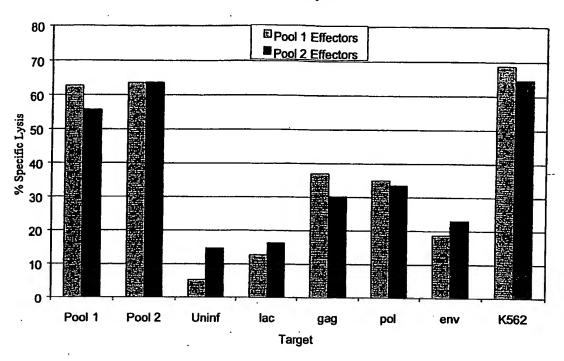


FIGURE 18C

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Subject1





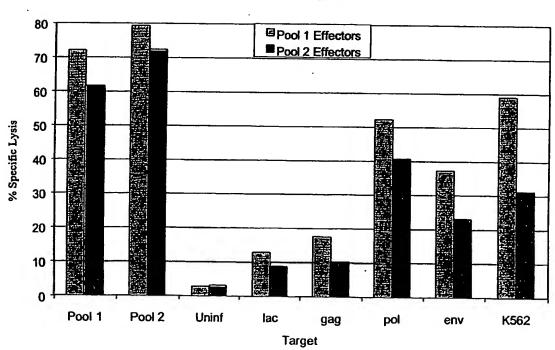


FIGURE 19

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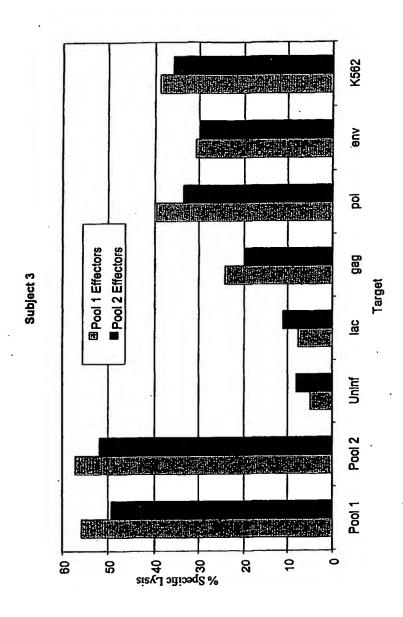


FIGURE 19 (Cont)

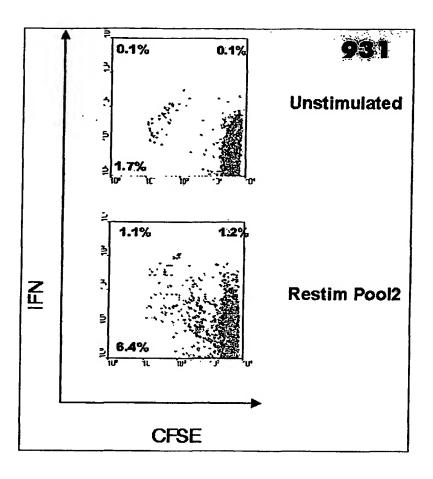


Figure 20

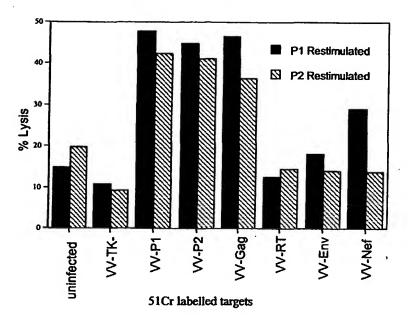


Figure 21

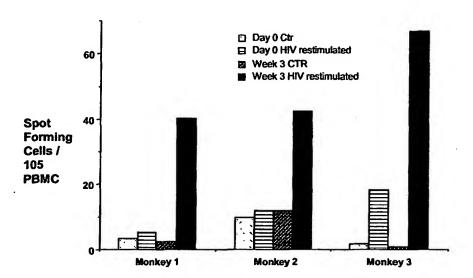


Figure 22A

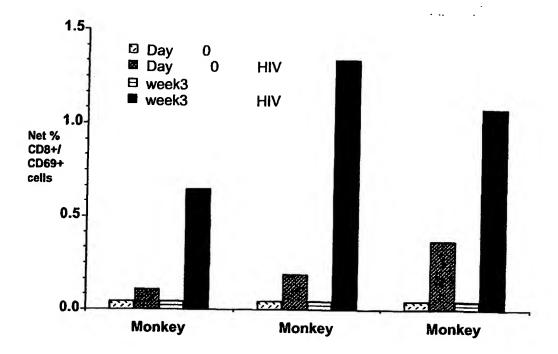


Figure 22B

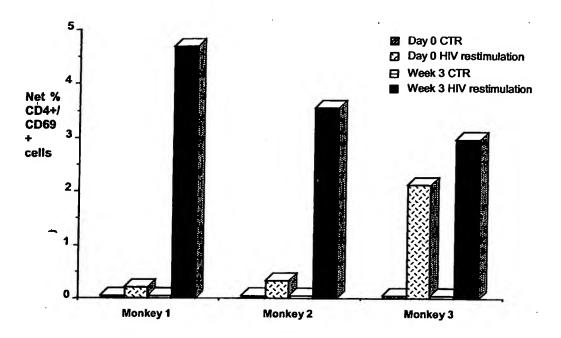


Figure 22C

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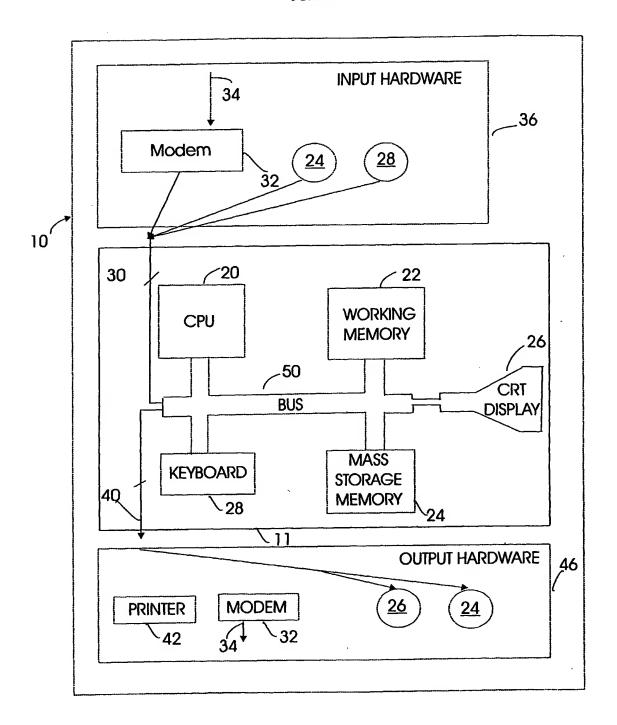


FIGURE 23

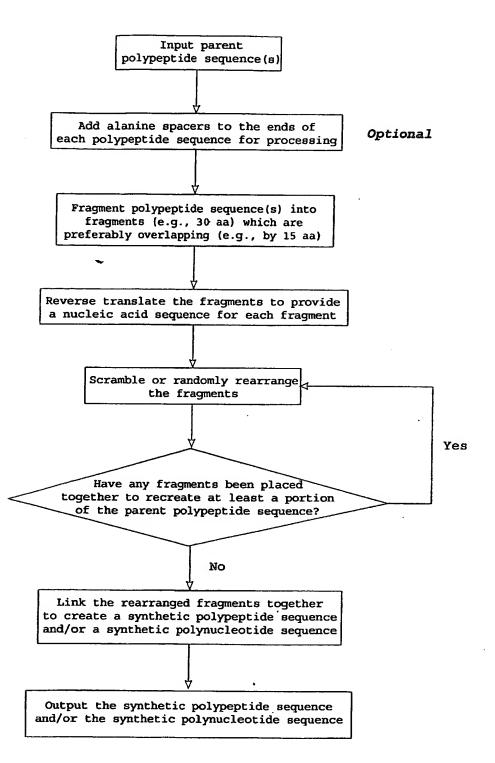


Figure 24

```
/* Scramble */
                                                      95/216
  /* Includes */
  #include <stdio.h>
  #include <stdlib.h>
  #include <string.h>
  #include <time.h>
 /* Constant definitions */
 /* Version Information */
 #define VERSION_NO
                                                                        "0.2"
 #define VERSION_DATE
                                                            "04/03/1999"
 /* Misc */
 #define KEYBOARD_BUFFER SIZE
                                                256
                                                                        /*size of keyboard read buffer */
 #define LEN_CODON
                                                                                    /*length of codon (including
 null) */
 #define BUFFER SIZE
                                                                        10000
                                                                                   /*size of file read buffer */
 #define TRUE
                                                                                               /*boolean true */
 #define FALSE
                                                                       0
                                                                                               /*boolean false */
 /* Error codes */
#define E_NOERROR
#define E_NOINFILE
#define E_MALLOC
#define E_FILEREAD
                                                           0
                                                                                   /*no error */
                                                            1
                                                                                   /*genes file not found */
                                                           2
                                                                                   /*memory allocation error */
                                                           3
                                                                                   /*file read error */
 #define E_CREATE_OUTPUT_FILE
                                                                       /*error creating output file */
 #define E OVERLAP
                                                           5
                                                                                   /*segment overlap >= length
/* Structure definitions */
typedef struct gene GENE;
typedef GENE * P_GENE;
typedef struct gene_segment GENE_SEGMENT;
typedef GENE_SEGMENT * P_GENE_SEGMENT:
struct gene {
            char * name;
            char * data;
            P_GENE next_gene;
};
struct gene_segment {
           P_GENE p_gene;
           int number;
           int offset;
           int first_codon_choice;
           char * amino data:
           char * dna data;
           P_GENE_SEGMENT next_seg;
}:
```

```
96/216
   /* Function prototypes */
   int prolog();
   int get parameters();
   int read_int(char * prompt);
   int load genes();
   int add gene(char * gene name,char * gene data);
   void insert_gene(P_GENE * head,P_GENE new_gene);
  int add_aa();
  int split_genes();
  int split_gene(P_GENE g);
  int insert_segment(P_GENE_SEGMENT * head_seg,P_GENE_SEGMENT new_seg);
  int convert segments aa to dna();
  int convert aa to dna(char * aa ptr,char * dna ptr,int first choice):
  char * codon(char acid_char,int preferred);
  int perform_scramble();
  int scramble segments();
  int adjacent segments();
  int display genes();
  int write_output_file();
  void strip_newline(char * strip_str);
  void pad_amino_string(char * amino_ptr, char * padded_ptr);
  int even(int test num);
 void read_str(char * prompt,char * string);
char * read_nonblank_line(char * buf,int buf_size,FILE * in_file);
 int user_confirmation();
 void test();
 /* Global variables */
 char * codon_table[26][2] = {
 /" A 00 "/ {"GCC","GCT"},
/" - 01 "/ {"???","???"},
/" C 02 "/ {"TGC","TGT"},
/" D 03 "/ {"GAC","GAT"},
 /" E 04 "/ {"GAG","GAA"},
 /" F 05 */ {"TTC","TTT"},
/" G 06 */ {"GGC","GGA"},
 /" H 07 */ {"CAC","CAT"},
/"108 */ ("ATC", "ATT"),
/"-09 */ ("???", "???"),
/" K 10 */ ("AAG", "AAA"),
/" L 11 */ ("CTG", "CTC"),
/" M 12 */ ("ATG", "ATG"),
/" N 13 */ ("AAC", "AAT"),
/" - 14 */ ("???" "????")
 /* - 14 */ {**???","???"},
 /" P 15 */ ("CCC", "CCT").
/" Q 16 "/ {"CAG","CAA"},
/" R 17 "/ {"AGG","AGA"},
/" S 18 "/ {"AGC","TCC"},
/" T 19 "/ {"ACC","ACA"},
/" - 20 "/ {"???","???"},
/" V 21 "/ {"GTG","GTC"},
/" W 22 "/ {"TGG","TGG"},
```

Figure 25 (Cont)

```
/" - 23 */ {"???","???"},
/" Y 24 */ {"TAC","TAT"},
                                                     97/216
 /* - 25 */ {"???","???"}
}:
char * error_text[] = {
/* 00 */ ···
/* 01 */ ,"ERROR: Input file not found!"
/* 02 */ ,"ERROR: Memory allocation error"
/* 03 */ ,"ERROR: File read error"
/* 04 */ ,"ERROR: Could not create output file"
/* 05 */ ,"ERROR: Segment overlap must be less than segment length"
char disease name[KEYBOARD BUFFER SIZE]:
char input_file_name[KEYBOARD_BUFFER_SIZE];
char output_file_name[KEYBOARD_BUFFER_SIZE];
int num genes = 0;
int num segments = 0;
int len segment;
int segment_overlap;
P_GENE first_gene = NULL;
P_GENE_SEGMENT first_segment = NULL;
P_GENE_SEGMENT * scrambled_segments = NULL;
/* Mainline */
void main() {
           int error = E_NOERROR;
           printf("Scramble - Version %s, %s\n\n", VERSION_NO, VERSION_DATE);
           /* Initial processing */
           if (!error)
                      error = prolog();
           /* Get various program parameters from user */
           if (!error)
                      error = get_parameters();
           /* Load genes from genes file */
           if (!error)
                      error = load genes();
           /* Add 'AA' to start and end of all genes */
           if (!error)
                      error = add_aa();
          /* Split genes into overlapping chunks */
          if (!error)
                      error = split_genes();
          /* Convert segment amino acid to dna */
          if (!error)
                      error = convert_segments_aa_to_dna();
```

Figure 25 (Cont)

```
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             /* Scramble the segments */
              if (!error)
                          error = perform_scramble();
             /* Write output file */
             if (!error)
                          error = write_output_file();
             /* Show error if there was one */
             if (error)
                         printf("%s\n",error text[error]);
 }
 /* prolog() */
 /* Perform any initial processing required */
 int prolog() {
             /* Seed the random number generator, using the system clock */
             /* Don't run the program more than once in the same second! */
             /* Or we'll get the same randomisation!!!!!!!!!!!!! */
             srand(time(NULL));
             return E NOERROR;
}
/* get_parameters() */
/* Ask for various parameters from the user (stdin) */
     Disease name
     Input file name
     Output file name
     Segment length
int get_parameters() {
            int valid;
            read_str("Enter disease name : ",disease_name);
read_str("Enter input file name : ",input_file_name);
read_str("Enter output file name : ",output_file_name);
            valid = FALSE;
            while (!valid) {
                         len_segment = read_int("Enter segment length : ");
                         if (len segment % 2)
                                     printf("Segment length must be even!\n");
                         else
                                     valid = TRUE;
            segment overlap = len_segment / 2;
            return E NOERROR;
/* load_genes() */
```

Figure 25 (Cont)

```
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/* Load the genes from the input file */
int load_genes() {
    FILE * input_file;
           char name_buf[BUFFER_SIZE];
           char data buf[BUFFER_SIZE];
           /* Open genes file for reading */
           if (NULL == (input file = fopen(input_file_name, "r")))
                      return E_NOINFILE;
           printf("Loading genes from: %s\n",input_file_name);
           num_genes = 0;
           /* Read gene name */
           while (NULL != read_nonblank_line(name_buf,BUFFER_SIZE,input_file)) {
                      /* Read the gene data */
                     if (NULL != read_nonblank_line(data_buf,BUFFER_SIZE,input_file)) {
                                 /* Allocate memory for new gene and add to list */
                                 if (rc = add_gene(name_buf,data_buf))
                     }
          /* Close genes file */
          fclose(input file);
          return rc;
}
/* add_gene() */
/* Allocate memory for new gene, then insert in list */
int add_gene(char * gene_name,char * gene_data) {
          P_GENE new_gene;
          /* Allocate storage for new gene */
          if (NULL == (new_gene = malloc(sizeof(GENE))))
                     return E_MALLOC;
          /* Initialise new gene */
          new gene->next gene = NULL;
          /* Allocate storage for gene name (+1 for null) */
          if (NULL == (new_gene->name = malloc(strlen(gene_name)+1)))
                     return E_MALLOC;
          /* Store gene name */
          strcpy(new gene->name,gene name);
          /* Allocate storage for gene data (+1 for null) */
          if (NULL == (new_gene->data = malloc(strlen(gene_data)+1)))
                     return E_MALLOC;
          /* Store gene data */
          strcpy(new_gene->data,gene_data);
          /* Insert the new gene into linked list */
          insert_gene(&first_gene,new_gene);
          /* Increment num genes */
          num_genes++;
```

Figure 25 (Cont)

```
return E_NOERROR;
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 }
 /* insert_gene() */
 /* Insert gene into linked list */
 void insert_gene(P_GENE * head_gene,P_GENE new_gene) {
            P_GENE * cur_ptr = head_gene;
           while (NULL != (*cur_ptr))
                      cur_ptr = &((*cur_ptr)->next_gene);
            *cur_ptr = new_gene;
}
/* add_aa() */
/* Add 'AA' to the start and end of every gene */
int add_aa() {
           P_GENE cur_gene = first_gene;
           char * new_data;
           while (NULL != cur_gene) {
                      /* Allocate storage to fit the gene plus four characters */
                      new_data = malloc(strien(cur_gene->data)+5);
                      /* Shift gene data to new storage, add "AA" */
                      strcpy(new_data,"AA");
                      strcat(new_data,cur_gene->data);
                      strcat(new_data,"AA");
                      /* Free previous gene data storage */
                      free(cur gene->data);
                      /* Set gene data pointer to new storage */
                      cur_gene->data = new_data;
                      /* Advance to next gene */
                      cur_gene = cur_gene->next_gene;
          }
          return E_NOERROR;
}
/* split_genes() */
/* Split the genes into overlapping segments */
int split_genes() {
          P_GENE cur_gene = first_gene;
          P_GENE_SEGMENT cur_seg = first_segment;
          printf("Splitting genes into segments...\n");
          /* Split the genes into segments */
          while (NULL != cur_gene) {
                     /* Split the gene */
                     split_gene(cur_gene);
                     /* Advance to next gene */
```

Figure 25 (Cont)

```
cur_gene = cur_gene->next_gene;
           }
           /* Count the number of segments */
           num_segments = 0;
           cur_seg = first_segment;
           while (NULL != cur_seg) {
                     num_segments++;
                     cur seg = cur seg->next seg:
           }
           return E_NOERROR;
/* split gene() */
/* Split a gene into overlapping segments */
P_GENE_SEGMENT new segment = NULL:
          int done;
          int seg_ctr = 0;
          /* Allocate memory for segment buffer */
          if (NULL == (seg_buf = malloc(len_segment+1)))
                    return E_MALLOC;
          I* Insert a null at the end of the segment buffer, */
          /* so we can use it as a string */
          seg_buf[len_segment] = '\0';
          /* Set segment pointer to start of gene data */
          seg_ptr = g->data;
          done = FALSE;
          while (!(done)) {
                    /* So we know if we copied data */
                    seg_buf[0] = '\0';
                   /* Copy a segment of gene data to the segment buffer */
                   memcpy(seg_buf,seg_ptr,len_segment);
                   /* If there was some gene data copied to the buffer */
                   if (NULL != seg_buf[0]) {
                              /* Allocate storage for a new segment */
                              if (NULL == (new_segment = malloc(sizeof(GENE_SEGMENT))))
                                         return E MALLOC;
                              /* Increment segment counter */
                              seg_ctr++;
                              /* Setup the new segment */
                              new_segment->p_gene = g;
                              new_segment->number = seg_ctr;
                              new_segment->offset = seg_ptr - g->data + 1;
                              new_segment->next_seg = NULL:
```

Figure 25 (Cont)

```
if (NULL == (new_segment->amino_data = malloc(len_segment+1)))
                                           return E MALLOC;
                                if (NULL == (new_segment->dna_data = malloc(len_segment*3+1)))
                                           retum E_MALLOC;
                                new_segment->amino_data[0] = '\0';
                                new_segment->dna_data[0] = 10;
                                /* Copy segment data from buffer to new segment */
                                strcpy(new_segment->amino_data,seg_buf);
                                /* Insert new segment into chain from gene */
                                insert_segment(&first_segment,new_segment);
                    `}
                      /* If we didn't read a full segment, we are finished! */
                     if (strlen(seg_buf) < len_segment)
                                done = TRUE:
                     /* Otherwise, advance segment pointer to next segment in buffer */
                                seg_ptr = seg_ptr + len_segment - segment overlap;
          }
}
/* insert_segment() */
/* Insert a segment node at the end of the list */
int insert_segment(P_GENE_SEGMENT * head_seg,P_GENE_SEGMENT new_seg) {
          P_GENE_SEGMENT * cur ptr = head seg;
          while (NULL != (*cur_ptr))
                     cur_ptr = &((*cur_ptr)->next_seg);
          *cur_ptr = new_seg;
/* convert_segments_aa_to_dna */
/* Go thru segments, and for each, convert amino acids to dna */
int first_choice = 1;
          int alternate;
          printf("Converting to DNA...\n");
          /* Work out if we need to alternate the first codon choice or not */
          /* Don't need to do this anymore, since the segment length is
          /* forced to be even, and the overlap is half the length (odd). */
          /*alternate = ((even(len_segment) && even(segment_overlap))
                               || (!even(len_segment) && !even(segment_overlap)));*/
          alternate = FALSE:
          while (NULL != cur_seg) {
                    cur_seg->first_codon_choice = first_choice;
                    convert_aa_to_dna(cur_seg->amino_data,cur_seg->dna_data,
                                                                        cur_seg->first_codon_choice);
```

```
/* Address next segment */
                         cur_seg = cur_seg->next_seg;
                         /* If we are alternating, alternate the first codon choice */
                         /*if (alternate)
                                    if (1 == first_choice)
                                                first_choice = 2;
                                    else
                                                first_choice = 1.*/
             }
             return E_NOERROR;
  }
  /* convert_aa_to_dna */
 /* Converts a string of amino acid to dna */
 /* NOTE: assumes that buffer at dna_ptr is large enough to hold dna!!! */
 int convert_aa_to_dna(char * aa_ptr,char * dna_ptr,int first_choice) {
             char * p_codon;
            int cur_preferred = first choice;
            while (10' != *aa_ptr) {
                        p_codon = codon(*aa_ptr,cur_preferred);
                        strcat(dna_ptr,p_codon);
                        /* If we didn't find a codon, log a warning */
                        if (0 == strcmp(p\_codon,"???\0"))
                                   printf("WARNING: no codon found for arnino acid!\n");
                       /* Alternate current preferred codon */
                       if (1 == cur_preferred)
                                   cur_preferred = 2;
                       else
                                   cur_preferred = 1;
                       aa_ptr++;
           return E_NOERROR;
/* codon */
/* Returns a pointer to a codon corresponding to the amino acid passed */
/* The codon pointer is to 3 characters, plus a terminating null */
char * codon(char acid_char,int preferred) {
           int codon_table_index;
           char * codon ptr;
           /* Determine index into codon_table (table starts at 'A') */
           codon_table_index = acid_char - 'A';
           /* Set pointer to appropriate codon */
           codon_ptr = codon_table[codon_table_index][preferred-1];
```

```
return codon_ptr;
 }
 /* display_genes() */
 /* Display the name and data for all genes */
 int_display_genes() {
            P_GENE cur_gene = first_gene;
            while (NULL != cur gene) {
                       printf("%s\n",cur_gene->name);
printf("%s\n",cur_gene->data);
                       cur_gene = cur_gene->next_gene;
            }
            return E_NOERROR;
 }
 /* perform scramble() */
 /* Scramble the segments */
 /* Check for adjacent segments. If there are, rescramble */
 int perform_scramble() {
           int done = FALSE;
           int rc = E_NOERROR;
           while (TRUE) {
                      rc = scramble_segments();
                      if (E_NOERROR == rc)
                                  if (adjacent_segments()) {
                                             printf("Adjacent segments detected! Rescramble? (y/n) ");
                                             if (!user_confirmation()) {
                                                        printf("WARNING: Adjacent segments in output
file.\n");
                                                        break;
                                            }
                                 else
                                            break;
                      else
                                 break;
           }
           return rc;
}
/* scramble segments() */
/* Randomly scramble the segments, putting pointers in scrambled segments[] */
int scramble_segments() {
          P_GENE_SEGMENT cur_seg = first_segment;
          P GENE SEGMENT temp;
          printf("Scrambling segments...\n");
```

Figure 25 (Cont)

```
/* Allocate storage for array of segment pointers */
            if (NULL == (scrambled_segments = malloc(sizeof(P GENE SEGMENT)*num segments)))
                       return E MALLOC;
            /* First, initialise scrambled_segments in same order as linked list */
            while (cur_seg != NULL) {
                       scrambled_segments[i] = cur_seg;
                       cur_seg = cur_seg->next_seg;
            }
            /* Now, randomly scramble the segments */
            for (i=0;i<num_segments;i++) {
                                   = rand() % num segments;
                                      = scrambled_segments[i];
                      scrambled_segments[i] = scrambled_segments[j];
                      scrambled segments[j] = temp;
           }
           return E_NOERROR;
}
/* adjacent_segments() */
/* Determine if the scrambled segment order has resulted in */
/* two segments which were adjacent originally (ie every */
/* second one) have ended up adjacent.
int adjacent_segments() {
           int i:
           int rc = 0;
           P_GENE_SEGMENT cur_seg;
           P_GENE_SEGMENT next_seg;
           for (i=0;i<num_segments-1;i++) {
                      /* Address current and next segments */
                      cur_seg = scrambled_segments[i];
                      next_seg = scrambled_segments[i+1];
                      /* Do segments come from same gene, and are two apart? */
                      if (((cur_seg->p_gene == next_seg->p_gene)
                                && ((cur_seg->number == (next_seg->number)+2)
                                           (cur_seg->number == (next_seg->number)-2))))
                                return 1:
           return 0;
/* write_output_file() */
/* Write out segments (in initial non-scrambled order) */
/* Write out synthetic protein (in scrambled order) */
/* Write out synthetic dna (in scrambled order) */
int write_output_file() {
          FILE * output file;
```

```
char * amino buffer;
 P GENE SEGMENT cur seg;
 int i;
 /* Open output file for writing (erase any contents) */
 if (NULL == (output_file = fopen(output_file_name, "w")))
             return E_CREATE_OUTPUT_FILE;
 /* Allocate memory for padded amino string buffer */
 if (NULL == (amino_buffer = malloc(len_segment*3+1)))
             return E_MALLOC;
 printf("Writing output file: %s\n".output file name);
 /* Write output file header information */
 fprintf(output_file,"Scramble %s - Output File\n", VERSION_NO);
fprintf(output_file,"\n");
fprintf(output_file,"Disease name : %s\n",disease_name);
 fprintf(output_file;"Input filename : %s\n",input file name);
fprintf(output_file,"Output filename : %s\n",output_file_name);
fprintf(output_file,"Number genes : %d\n",num_genes);
fprintf(output file,"Number segments: %d\n",num segments);
fprintf(output_file, "Segment length : %d\n", len_segment);
fprintf(output_file,"Segment overlap : %d\n",segment_overlap);
/* Write out segments in initial non-scrambled order */
fprintf(output_file,"\n");
fprintf(output_file, "Segments in original order:\n");
fprintf(output file,"-
cur seg = first segment;
while (NULL != cur_seg) {
            /* Format amino data to line up with codons */
            pad_amino_string(cur_seg->amino_data,amino_buffer);
            fprintf(output_file,"Gene : %s\n",cur_seg->p_gene->na
fprintf(output_file,"Segment# : %d\n",cur_seg->number);
fprintf(output_file,"Offset : %d\n",cur_seg->offset);
                                        : %s\n",cur_seg->p_gene->name);
            fprintf(output_file,"1st Codon: %d\n",cur_seg->first_codon_choice);
            fprintf(output_file, "%s\n", amino_buffer);
            fprintf(output_file, "%s\n", cur seg->dna data);
            fprintf(output file,"\n");
            cur seg = cur seg->next_seg;
/* Write out segment names in scrambled order */
fprintf(output_file, "Segments in scrambled order:\n");
fprintf(output_file "--
for (i=0;i<num_segments;i++) {
            /* Format amino data to line up with codons */
            pad_amino_string(scrambled_segments[i]->amino_data,amino_buffer);
            /* Write segment details */
            fprintf(output_file,"%s #%d\n",scrambled_segments[i]->p_gene->name,
                       scrambled segments[i]->number);
            fprintf(output file,"%s\n",amino buffer);
            fprintf(output file, "%s\n", scrambled segments[i]->dna data);
           fprintf(output_file,"\n");
```

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```
}
             /* Write synthetic protein in one long string */
             fprintf(output_file, "Synthetic Protein:\n");
             fprintf(output_file,"--
             for (i=0;i<num_segments;i++)
                        fprintf(output_file,"%s",scrambled_segments[i]->amino data);
             fprintf(output_file,"\n\n");
            /* Write synthetic dna in one long string */
             fprintf(output_file,"Synthetic DNA:\n");
             fprintf(output_file,"-----
                                         ---\n*);
            for (i=0;i<num_segments;i++)
                        fprintf(output_file, "%s", scrambled_segments[i]->dna_data);
            retum E_NOERROR;
 }
 /* strip_newline() */
 /* Replace the first newline character with a null */
 void strip_newline(char * strip_str) {
            char * newline pos;
            /* Find the newline char */
            newline pos = strchr(strip str,\n');
            /* If we found one, replace it with a null */
            if (NULL != newline_pos)
                       newline pos[0] = \0';
}
/* pad_amino_string */
/* Copy amino chars from amino_ptr to padded_ptr, padding each */
/* side with a space. */
void pad_amino_string(char * amino_ptr, char * padded_ptr) {
           while ('\0' != *amino_ptr) {
                       *padded_ptr = ' ':
                       padded_ptr++;
                       *padded_ptr = *amino_ptr;
                       padded_ptr++;
                       *padded_ptr = ' ';
                       padded ptr++;
                       amino_ptr++;
           }
           /* Stick a null at the end of the padded string */
           *padded ptr = '\0';
}
/* even() */
/* True if test_num is even, otherwise false */
```

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```
int even(int test_num) {
             return !(test_num % 2);
  }
  /* read_int() */
  /* Read an integer from stdin. Keep trying until valid int > 0 entered. */
 /* Return the integer read, or 0 if error reading from stdin. */
 int read_int(char * prompt) {
             char buffer[KEYBOARD_BUFFER_SIZE];
            int value_read;
            int valid = FALSE;
            while (!valid) {
                        printf("%s",prompt);
                        valid = TRUE;
                        fgets(buffer,KEYBOARD_BUFFER_SIZE,stdin);
                        if (1 != sscanf(buffer, "%d", &value_read))
                                 valid = FALSE;
                        if (valid && (value_read < 1))
                                   valid = FALSE:
                        if (!valid)
                                   printf("Positive integer value please!\n");
            }
            return value read;
}
/* read_str() */
/* Read a string from the user (stdin) */
/* Strip the newline from it */
void read_str(char * prompt,char * string) {
            char buffer[KEYBOARD_BUFFER_SIZE];
            printf(prompt);
            fgets(buffer,KEYBOARD_BUFFER_SIZE,stdin);
            sscanf(buffer, "%s", string);
}
/* read_nonblank_line() */
/* Read a line from file until we get a non-blank one */
char * read_nonblank_line(char * buf,int buf size,FILE * in file) {
           char * return_ptr;
           /* Read lines until we get a non-black one, or EOF */
                       return_ptr = fgets(buf,buf_size,in_file);
           while ((NULL != return_ptr) && (('\n' == buf[0]) || (' ' == buf[0])));
           /* If we got a line, change the newline char to a null */
           if (NULL != return_ptr)
                      strip_newline(buf);
```

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HepC Savine design

HepC la consensus polyprotein sequence used for scramble program

MSTNPKPQRKTKRNTNRRPQDVKFPGGGQIVGGVYLLPRRGPRLGVRATRKTSERSQPRGRRQPIPKARRPEGRTWAQ PGYPWPLYGNEGCGWAGWLLSPRGSRPSWGPTDPRRRSRNLGKVIDTLTCGFADLMGYIPLVGAPLGGAARALAHGVR VLEDGVNYATGNLPGCSFSIFLLALLSCLTVPASAYQVRNSTGLYHVTNDCPNSSIVYEAADAILHTPGCVPCVREGN ASRCWVAMTPTVATRDGKLPATQLRRHIDLLVGSATLCSALYVGDLCGSVFLVGQLPTFSPRRHWTTQGCNCSIYPGH ITGHRMAWDMMNWSPTAALVMAQLLRIPQAILDMIAGAHWGVLAGIAYFSMVGNWAKVLVVLLLFAGVDAETHVTGG NAGRTTSGLVSLLTPGAKQNIQLINTNGSWHINSTALNCNESLNTGWLAGLFYQHKFNSSGCPERLASCRRLTDFDOG WGPISYANGSGPDQRPYCWHYPPKPCGIVPAKSVCGPVYCFTPSPVVVGTTDRSGAPTYSWGANDTDVFVLNNTRPPL GNWFGCTWMNSTGFTKVCGAPPCVIGGAGNNTLHCPTDCFRKHPEATYSRCGSGPWITPRCLVDYPYRLWHYPCTINY TIFKVRMYVGGVEHRLEAACNWTRGERCDLEDRDRSELSPLLLSTTQWQVLPCSFTTLPALSTGLIHLHQNIVDVQYL YGVGSSIASWAIKWBYVVLLFLLLADARVCSCLWMMLLISQAEAALENLVILNAASLAGTHGLVSFLVFFCFAWYLKG RWVPGAVYALYGMWPLLLLLLALPQRAYALDTEVAASCGGVVLVGLMALTLSPYYKRYISWCLWWLQYFLTRVEAQLH VWVPPLNVRGGRDAVILLMCVVHPTLVFDITKLLLAVFGPLWILQASLLKVPYFVRVQGLLRICALARKMIGGHYVQM AIIKLGALTGTYVYNHLTPLRDWAHNGLRDLAVAVEPVVFSQMETKLITWGADTAACGDIINGLPVSARRGREILLGP ADGMVSKGWRLLAPITAYAQQTRGLLGCIITSLTGRDKNQVEGEVQIVSTAAQTFLATCINGVCWTVYHGAGTRTIAS PKGPVIQMYTNVDQDLVGWPAPQGSRSLTPCTCGSSDLYLVTRHADVIPVRRRGDSRGSLLSPRPISYLKGSSGGPLL CPAGHAVGIFRAAVCTRGVAKAVDFIPVENLETTMRSPVFTDNSSPPAVPQSFQVAHLHAPTGSGKSTKVPAAYAAOG YKVLVLNPSVAATLGFGAYMSKAHGIDPNIRTGVRTITTGSPITYSTYGKFLADGGCSGGAYDIIICDECHSTDATSI LGIGTVLDQAETAGARLVVLATATPPGSVTVPHPNIEEVALSTTGEIPFYGKAIPLEVIKGGRHLIFCHSKKKCDELA $\textbf{AKLVALGINAVAYYRGLDVSVIPTSGDVVVVATDALMTGYTGDFDSVIDCNTCVTQTVDFSLDPTFTIETTTLPQDAV$ SRTQRRGRTGRGKPGIYRFVAPGERPSGMFDSSVLCECYDAGCAWYELTPAETTVRLRAYMNTPGLPVCQDHLEFWEG VFTGLTHIDAHFLSQTKQSGENFPYLVAYQATVCARAQAPPPSWDQMWKCLIRLKPTLHGPTPLLYRLGAVQNEVTLT ${\tt HPVTKYIMTCMSADLEVVTSTWVLVGGVLAALAAYCLSTGCVVIVGRIVLSGKPAIIPDREVLYREFDEMEECSQHLP}$ YIEQGMMLAEQFKQKALGLLQTASRQAEVIAPAVQTNWQKLEVFWAKHMWNFISGIQYLAGLSTLPGNPAIASLMAFT AAVTSPLTTSQTLLFNILGGWVAAQLAAPGAATAFVGAGLAGAAIGSVGLGKVLVDILAGYGAGVAGALVAFKIMSGE VPSTEDLVNLLPAILSPGALVVGVVCAAILRRHVGPGEGAVQWMNRLIAFASRGNHVSPTHYVPESDAAARVTAILSS LTVTQLLRRLHQWISSECTTPCSGSWLRDIWDWICEVLSDFKTWLKAKLMPQLPGIPFVSCQRGYKGVWRGDGIMHTR CHCGAEITGHVKNGTMRIVGPRTCRNMWSGTFPINAYTTGPCTPLPAPNYTFALWRVSAEEYVBIRRVGDFHYVTGMT TDNLKCPCQVPSPEFFTELDGVRLHRFAPPCKPLLREEVSFRVGLHEYPVGSQLPCEPEPDVAVLTSMLTDPSHITAE AAGRRLARGSPPSMASSSASQLSAPSLKATCTANHDSPDAELIEANLLWRQEMGGNITRVESENKVVILDSFDPLVAE EDEREISVPABILRKSRRFAQALPVWARPDYNPPLVETWKKPDYEPPVVHGCPLPPPRSPPVPPPRKKRTVVLTESTL STALAKLATKSFGSSSTSGITGDNTTTSSEPAPSGCPPDSDAESYSSMPPLEGEPGDPDLSDGSWSTVSSEAGTEDVV CCSMSYSWTGALVTPCAAEEQKLPINALSNSLLRHHNLVYSTTSRSACQRQKKVTFDRLQVLDSHYQDVLKEVKAAAS KVKANLLSVEBACSLTPPHSAKSKFGYGAKDVRCHARKAVAHINSVWKDLLEDSVTPIDTTIMAKNEVFCVOPEKGGR KPARLIVFPDLGVRVCEKMALYDVVSKLPLAVMGSSYGFQYSPGQRVEFLVQAWKSKKTPMGFSYDTRCFDSTVTESD IRTERAIYQCCDLDPQARVAIKSLTERLYVGGPLTNSRGENCGYRRCRASGVLTTSCGNTLTCYIKARAACRAAGLQDCTMLVCGDDLVVICESAGVQEDAASLRAFTEAMTRYSAPPGDPPQPEYDLELITSCSSNVSVAHDGAGKRVYYLTRDP TTPLARAAWETARHTPVNSWLGNIIMFAPTLWARMILMTHFFSVLIARDQLEQALDCEIYGACYSIEPLDLPPIIQRL HGLSAFSLHSYSPGEINRVAACLRKLGVPPLRAWRHRARSVRARLLARGGRAAICGKYLFNWAVRTKLKLTPIAAAGR LDLSGWFTAGYSGGDIYHSVSHARPRWFWFCLLLLAAGVGIYLLPNR

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Scramble - Output Pile
Scramble version : 0.1 beta, 08/02/1999
             : 1
Num. genes
               : 201
Num. segments
              : 30
Segment length
Segment overlap : 15
Segments in original order:
Gene ·
        : HepCla
Segment# : 1
Offset
         : 1
1st Codon : 1
A A M S T N P K P Q R K T K R N T N R R P O D V K F P G G G
GCCGCTATGTCCACCAATCCCAAACCCCAAAGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAGACGTCAAGTTTCCCGGAGGCGGA
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: HepCla Segment# : 2 Offset : 16 1st Codon : 1 NTNRRPQDVKPPGGGQIVGGVYLLPRRGPR AACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTGGCGGAGGCCAAATCGTCGGCGGAGTGTATCTGCTCCCCAGAAGGGGACCCAGA Gene : HepCla Segment# : 3 Offset : 31 1st Codon : 1 Q I V G G V Y L L P R R G P R L G V R A T R K T S E R S Q P CAGATTGTGGGAGGCGTCTACCTCCTGCCTAGGAGAGGCCCTAGGCTCGGGGTCACGGGCTACCAGAAAGACAAGCGAAAGGTCCCAGCCT Gene : HepCla Segment# : 4 Offset : 46 LGVRATRKTSERSQPRGRRQPIPKARRPEG CTGGGAGTGAGAGCCACAAGGAAAACCTCCGAGAGAAGCCAACCCAGAGGCAGAAGGCAAACCCATTCCCAAAGCCAGAAGGCTGAGGGA Gene : HepCla Segment# : 5 Offset : 61 1st Codon : 1 R G R R Q P I P K A R R P B G R T W A Q P G Y P W P L Y G N AGGGGAAGGAGACAGCCTATCCCTAAGGCTAGGAGACCCGAAGGCAGAACCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAAT : HepCla Segment# : 6 : 76 Offset 1st Codon : 1 R T W A Q P G Y P W P L Y G N E G C G W A G W L L S P R G S AGGACATGGGCTCAGCCTGTCCCTGGCCCCTCTACGGAAACGAAGGCTGTGGCTGGGCCGGATGGCTCCTGTCCCCCAGAGGCTCC Gene : HepCla Segment# : 7 Offset : 91 1st Codon : 1 EGCGWAGWLLSPRGSRPSWGPTDPRRRSRN GAGGGATGCGGATGGCTGGCTGCTCAGCCCTAGGGGAAGCAGACCCTCCTGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAAT Gene : HepCla Segment# : 8 Offset : 106 1st Codon : 1 R P S W G P T D P R R R S R N L G K V I D T L T C G F A D L AGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACACTGACATGCGGATTCGCTGACCTC : HepCla Segment# : 9 Offset : 121 1st Codon : 1 LGKVIDTLTCGPADLMGYIPLVGAPLGGAA $\tt CTGGGAAAGGTCATCGATACCCTCACCTGTGGCTTTGCCGATCTGATGGGCTATATCCCTCTGGTCGGCGCTCCCCTCGGCGGAGCCGCT$: HepCla Segment# : 10 Offset : 136 1st Codon : 1 MGYIPLVGAPLGGAARALAHGVRVLEDGVN ATGGGATACATTCCCCTCGTGGGAGCCCCTCTGGGAGGGCGCTGCCAGGCCCTCGCCCATGGCGTCAGGGTCCTGGAAGACGGAGTGAAT : HepCla

Segment# : 11 Offset : 151 1st Codon : 1 RALAHGVRVL B D G V N Y A T G N L P G C S P S I F L AGGGCTCTGGCTCACGGAGTGGCGTCGAGGATGGCGTCAACTATGCCACAGGCAATCTGCCTGGCTGTAGCTTTTAGCATTTTCCTC

Gene : HepCla Segment# : 12 Offset : 166

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1st Codon : 1 Y A T G N L P G C S F S I F L L A L L S C L T V P A S A Y Q TAGGCTACCGGAAACCTCCCCGGATGCTCCTTCTCCATCTTTCTGCTCGCCCTCCTGTCCTGCCTCACCGTCCCCGCTAGCGCTTACCAA : HepCla Gene Segment# : 13 Offset : 181 1st Codon : 1 L A L L S C L T V P A S A Y Q V R N S T G L Y H V T N D C P CTGGCTCTGCTCAGCTGTCTGACAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAAACGATTGCCCT Gene : HepCla Segment# : 14 Offset : 196 1st Codon : 1 V R N S T G L Y H V T N D C P N S S I V Y E A A D A I L H T GTGAGAAACTCCACCGGACTGTATCACGTCACCAATGACTGTCCCCAATAGCTCCATCGTCTACGAAGCCGCTGACGCTATCCTCCACACA Gene : HepCla Segment# : 15 Offset : 211 1st Codon : 1 N S S I V Y E A A D A I L H T P G C V P C V R E G N A S R C AACTCCAGCATTGTGTATGAGGCTGCCGATGCCATTCTGCATACCCCTGGCTGTGTGCCTTGCGTCAGGGAAGGCAATGCCTCCAGGTGT Gene : HepCla Segment# : 16 Offset. : 226 1st Codon : 1 P G C V P C V R B G N A S R C W V A M T P T V A T R D G K L CCCGGATGCGTCCCCTGTGTGAGAGAGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCACAGTGGCTACCAGAGACGGAAAGCTC : HepCla Gene Segment# : 17 Offset : 241 1st Codon : 1 WVAMTPTVATRDGKLPATQLRRHIDLLVGS Gene : HepCla Segment# : 18 Offset : 256 1st Codon : 1 PATQLRRHIDLLVGSATLCSALYVGD CGS CCCGCTACCCAACTGAGAAGGCATATCGATCTGCTCGTGGGAAGCGCTACCCTCTGCTCCGCCCTCTACGTCGGCGATCTGTTGGGCTCC Gene . : HepCla Segment# : 19 Offset : 271 1st Codon : 1 A T L C S A L Y V G D L C G S V F L V G Q L P T F S P R R H GCCACACTGTGTAGCGCTCTGTATGTGGGAGACCTCTGCGGAAGCGTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGCAT Gene : HepCla Segment# : 20 Offset : 286 1st Codon : 1 V F L V G Q L F T F S P R R H W T T Q G C N C S I Y P G H I GTGTTTCTGGTCGGCCAACTGTTTACCTTTAGCCCTAGGAGACACTGGACCACACAGGGATGCAATTGCTCCATCTTATCCCGGACACATT Gene : HepCla Segment# : 21 Offset : 301 1st Codon : 1 W T T Q G C N C S I Y P G H I T G H R M A W D M M M N W S P TGGACAACCCAAGGCTGTAACTGTAGCATTTACCCTGGCCATATCACAGGCCATAGGATGGCCTGGGACATGATGAACTGGAGCCCT Gene : HepCla Segment# : 22 Offset : 316 1st Codon : 1 T G H R M A W D M M M N W S P T A A L V M A Q L L R I P Q A ACCGGACACAGAATGGCTTGGGATATGATGATGATGATTGGTCCCCCACAGCCGCTCTGGTCATGGCTCAGCCTCCTGAGAATCCCTCAGGCT

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: HepCla Segment# : 23 Offset : 331 1st Codon : 1 TAALVMAQLLRIPQAILDMIAGAHWGVLAG ACCECTGCCCTCGTGATGCCCCAACTGCTCAGGATTCCCCAAGCCATTCTGGATATGATTGCCGGAGCCCATTGGGGAGTGCTCGCCGGA : HepCla Segment# : 24 Offset : 346 1st Codon : 1 I L D M I A G A H W G V L A G I A Y F S M V G N W A K V L V : HepCla Segment# : 25 Offset : 361 1st Codon : 1 I A Y P S M V G N W A K V L V V L L F A G V D A E T H V T ATCGCTTACTTTAGCATGGTGGGAAACTGGCCCAAAGTGCTCGTGGTCCTGCTCTGTTTGCCGGAGTGGATGCCGAAACCCATGTGACA Gene : HepCla Segment# : 26 Offset : 376 1st Codon : 1 V L L F A G V D A E T H V T G G N A G R T T S G L V S L L GTGCTCCTGCTCTTCGCTGGCGTCGACGCTGACGCACACGTCACCGCGGGCAATGCCGGAAGGACAACCTCCGGCCTCGTGTCCCTGCTC : HepCla Segment# : 27 1st Codon : 1 G G N A G R T T S G L V S L L T P G A K Q N I Q L I N T N G GGCGCAAACGCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCCGGAGCCAAACAGAATATCCAACTGATTAACACAAACGGA Gene : HepCla Segment# : 28 : 406 Offset 1st Codon : 1 T P G A K Q N I Q L I N T N G S W H I N S T A L N C N E S L ACCCCTGGCGCTAAGCAAAACATTCAGCTCATCAATACCAATGGCTCCTGGCATATCAATAGCACAGCCCTCAACTGTAACGAAAGCCTC Gene : HepCla Segment# : 29 Offset : 421 1st Codon : 1 S W H I N S T A L N C N B S L N T G W L A G L P Y Q H K P N AGCTGGCACATTAACTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACAAATTCAAT Gene : HepCla Segment# : 30 Offset : 436 N T G W L A G L P Y Q H K F N S S G C P E R L A S C R R L T AACACGGCTGGCTGGCCTCTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCCTGAGAGACTGGCTAGCTGTAGGAGACTGACA : HepCla Segment# : 31 Offset : 451 1st Codon : 1 S S G C P B R L A S C R R L T D P D Q G W G P I S Y A N G S AGCTCCGGCTGTCCCGAAAGGCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGGATGGGGACCCATTAGCTATGCCAATGGCTCC : HepCla Segment# : 32 Offset : 466 1st Codon : 1 D P D Q G W G P I S Y A N G S G P D Q R P Y C W H Y P P K P GACTTTGACCAAGGCTGGGGCCCTATCTCCTACGCTAACGGAAGCGGACCCGATCAGAGACCCTATTGCTGGCACTATCCCCCTAAGCCT : HepCla

Gene : HepCla Segment# : 33

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Offset : 481 1st Codon : 1 G P D Q R P Y C W H Y P P K P C G I V P A K S V C G P V Y C GGCCCTGACCAAAGGGCCTTACTGTTGGCATTACCCTCCCAAACCCTGTGGCATTGTGCCTACAAAAGCGTCTGCGGACCCGTCTACTGT Gene : HepCla Segment# : 34 Offset : 496 1st Codon : 1 C G I V P A K S V C G P V Y C P T P S P V V G T T D R S G Gene : HepCla Segment# : 35 Offset : 511 1st Codon : 1 PTPSPVVGTTDRSGAPTYSWGANDTDVPV TTCACACCCTCCCCGTGGTGGGCACAACCGATAGGTCCGGCGCTCCCACATACTCCTGGGGAGCCAATGACACAGACGTCTTCGTC Gene : HepCla Segment# : 36 : 526 1st Codon : 1 A P T Y S W G A N D T D V P V L N N T R P P L G N W P G C T GCCCCTACCTATAGCTGGGGCGCTAACGATACCGATGTGTTTGTGCTCAACAATACCAGACCCCCTCTGGGAAACTGGTTCGGATGCACA Gene : HepCla Segment# : 37 Offset : 541 1st Codon : 1 LNNTRPPLGNWPGCTWMNSTGPTKVCGAPP CTGAATAACACAAGGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCT Gene : HepCla Segment# : 38 : 556 Offset 1st Codon : 1 W M N S T G F T K V C G A P P C V I G G A G N N T L H C P T Gene : HepCla Segment# : 39 Offset : 571 1st Codon: 1 CVIGGAGNNTLHCPTDCFRKHPBATYSRCG TEGETCATCEGAGGCECTGCCAATAACACACTGCATTGCCCTACCGATTGCTTTAGGAAACACCCTGAGGCTACCTATAGCAGATGCGGA Gene : HepCla Segment# : 40 1st Codon : 1 DCFRKHPBATYSRCGSGPWITPRCLVDYPY GACTGTTTCAGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTCGACTATCCCTAT Gene : HepCla Segment# : 41 Offset : 601 SGPWITPRCLVDYPYRLWHYPCTINYTIPK AGCGGACCCTGGATCACACCCAGATGCCTCGTGGATTACCCTTACAGACTGTGGCACTATCCCTGTACCATTAACTATACCATTTTCAAA Gene : HepCla : 42 Segment# : 616 1st Codon : 1 RLWHYPCTINYTIFKVRMYVGGVEHRLEAA AGGCTCTGGCATTACCCTTGCACAATCAATTACACAATCTTTAAGGTCAGGATGTACGTCGGCGGAGTGGAACACAGACTGGAAGCCCGCT Gene : HepCla Segment# : 43 Offset : 631 1st Codon : 1 V R M Y V G G V E H R L B A A C N W T R G E R C D L B D R D

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GTGAGAATGTATGTGGGAGGCGTCGAGGATAGGCTCGAGGCTGCCTGTAACTGGACCAGAGGCGGAAAGGTGTGACCTCGAGGATAGGGAT Gene : HepCla Segment# : 44 Offset : 646 1st Codon : 1 C N W T R G R R C D L E D R D R S E L S P L L S T T Q W Q TGCAATTGGACAAGGGGAGAGAGATGCGATCTGGAAGACAGAGACAGAGCGAACTGTCCCCCCTCCTGCTCAGCACAACCCAATGGCAA Gene : HepCla Segment# : 45 Offset : 661 1st Codon : 1 R S E L S P L L S T T Q W Q V L P C S F T T L P A L S T G AGGTCCGAGCTCAGCCCTCTGCTCCACCACACAGTGGCAGGTCCTGCCTTGCTCCTTCACAACCCTCCCCGCTCTGCCCCCGGA Gene : HepCla Segment# : 46 Offset : 676 1st Codon : 1 V L P C S P T T L P A L S T G L I H L H Q N I V D V O Y L Y Gene : HepCla Segment# : 47 Offset : 691 1st Codon : 1 LIHLHQNIVDVQYLYGVGSSIASWAIKWEY CTGATTCACCTCCACCAAAACATTGTGGATGTGCAATACCTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTAT : HepCla Gene Segment# : 48 Offset : 706 1st Codon : 1 G V G S S I A S W A I K W E Y V V L L F L L L A D A R V C S GGCGTCGGCTCCAGCATTGCCTCCTGGGCTATCAAATGGGAATACGTCGTGCTCCTGGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCC Gene : HepCla Segment# : 49 Offset : 721 1st Codon : 1 V V L L F L L A D A R V C S C L W M M L L I S Q A E A A L : HepCla Gene Segment# : 50 Offset : 736 1st Codon : 1 C L W M M L L I S Q A B A A L B N L V I L N A A S L A G T H TGCCTCTGGATGATGCTCCTGATTAGCCAAGCCGAAGCCGCTCTGGAAAACCTCGTGATTCTGAATGCCGCTAGCCTCGCCGGAACCCAT : HepCla Segment# : 51 Offset : 751 1st Codon : 1 B N L V I L N A A S L A G T H G L V S P L V F P C P A W Y L GAGAATCTGGTCATCCTCAACGCTGCCTCCCTGGCTGGCACACGCGCTCGGTCAGCTTTCTGGTCTTCTTTTGCCTTGGTCACCTC : HepCla Segment# : 52 : 766 Offset 1st Codon : 1 G L V S P L V F F C F A W Y L K G R W V P G A V Y A L Y G M GGCCTCGTGTCCTTCCTCGTGTTTTTCTGTTTCGCTTGGTATCTGAAAGGCAGATGGGTCCCCGGAGCCGTCTACGCTCTGTATGGCATG : HepCla Segment# : 53 Offset : 781 1st Codon : 1 K G R W V P G A V Y A L Y G M W P L L L L L A L P Q R A Y AAGGGAAGGTGGCCTGGCGCTGTTATGCCCTCTACGGAATGTGGCCCCTCCTGCTCCTGCTCCTGGCCTCAGAGAGCCCTAT

Gene : HepCla

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Segment# : 54 Offset : 796 1st Codon : 1 W P L L L L L A L P Q R A Y A L D T E V A A S C G G V V L $\tt TGGCCTCTGCTCCTGCTCCCCCAAAGGGCTTACGCTCTGGATACCGAAGTGCCTCCTCCGGAGGGGTTCGTGCTC$: HepCla Segment# : 55 Offset : 811 1st Codon : 1 A L D T E V A A S C G G V V L V G L M A L T L S P Y Y K R Y GCCCTCGACACAGAGGTCGCCGCTAGCTGTGGCGGAGTGGTCCTGGTCGGCCTCATGGCTCTGACACTGTCCCCCTATTACAAAAGGTAT : HepCla Segment# : 56 Offset : 826 1st Codon : 1 V G L M A L T L S P Y Y K R Y I S W C L W W L Q Y F L T R V GTGGGACTGATGCCCTCACCCTCACCCTTACTATAAGAGATACATTAGCTGGTGCCTCGGTGCCTGCAATACTTTCTGACAAGGGTC : HepCla Segment# : 57 Offset : 841 1st Codon : 1 I S W C L W W L Q Y F L T R V B A Q L H V W V P P L N V R G ATCTCCTGGTGTCTGTGGTGGCTCCAGTATTTCCTCACCAGAGTGGAAGCCCAACTGCATGTGGGTGCCTCCCCTCAACGTCAGGGGA : HepCla Segment# : 58 : 856 1st Codon : 1 BAQLHVWVPPLNVRGGRDAVILLMCVVHPT GAGGCTCAGCTCCACGTCTGGGTCCCCCCTCTGAATGTGAGAGGCGGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGTGCATCCCACA Gene : HepCla Segment# : 59 Offset : 871 G R D A V I L L M C V V H P T L V F D I T K L L A V F G P GGCAGAGACGCTGTGATTCTGCTCATGTGTGTGTCCACCCTACCCTCGTGTTTGACATTACCAAACTGCTCCTGGCTGTGTTTGGCCCT Gene : HepCla Segment# : 60 Offset : 886 1st Codon : 1 L V F D I T K L L A V F G P L W I L Q A S L L K V P Y F V CTGGTCTTCGATATCACAAAGCTCCTGCCGTCTTCGGACCCCTCTGGATTCTGCAAGCCTCCTGCTCAAGGTCCCCTATTTCGTC Gene : HepCla Segment# : 61 Offset : 901 1st Codon : 1 LWILQASLLKVPYPVRVQGLLRICALARKM CTGTGGATCCTCCAGGCTAGCCTCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAGATG : HepCla Segment# : 62 : 916 1st Codon : 1 R V Q G L L R I C A L A R K M I G G H Y V Q M A I I K L G A AGGGTCCAGGGACTGCTCAGGATTTGCGCTCTGGCTAGGAAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGCT : HepCla Segment# : 63 Offset : 931 1st Codon : 1 I G G H Y V Q M A I I K L G A L T G T Y V Y N H L T P L R D ATCGGAGGCCATTACGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATCTGACACCCCTCAGGGAT : HepCla

Gene : HepCla Segment# : 64 Offset : 946 1st Codon : 1

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LTGTYVYN H LTPLRDWAHNGLRDLAVAV B P CTGACAGGCACATACGTCTACAATCACCTCACCCCTCTGAGAGACTGGGCCCATAACGGACTGAGAGACCTCGCCGTCGAGCCT : HepCla Segment# : 65 Offset : 961 1st Codon : 1 WAHNGLRDLAVAVEPVVFSQMETKLITWGA TGGCTCACAATGGCCTCAGGGATCTGGCTGTGGCAGGACCCGTCGTCTTTAGCCAAATGGAAACCAAACTGATTACCTGGGGCGCGCT : HepCla Gene Segment# : 66 Offset : 976 1st Codon : 1 V V F S Q M B T K L I T W G A D T A A C G D I I N G L P V S GTGGTCTTCTCCCAGATGGAGACAAGCTCATCACATGGGGAGCCGATACCGCTGCCTGTCGCGATATCATTAACGGACTGCCTTGTGTCC : HepCla Gene Segment# : 67 Offset : 991 1st Codon : 1 DTAACGDIINGLPVSARRGREILLGPADGM Gene : HepCla Segment# : 68 Offset : 1006 1st Codon : 1 ARRGREILLGPADGMVSKGWRLLAPITAYA GCCAGAAGGGGAAGGGAAATCCTCCTGGGACCCGCTGACGGAATGGTCAGCAAAGGCTGGAGGCTCCTGGCTCCCATTACCGCTTACGCT : HepCla Gene Segment# : 69 Offset : 1021 1st Codon : 1 V S K G W R L L A P I T A Y A Q Q T R G L L G C I I T S L T GTGTCCAAGGGATGGAGACTGCTCGCCCCTATCACAGCCTATGCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCCTGACA Gene : HepCla Segment# : 70 Offset : 1036 1st Codon : 1 Q Q T R G L L G C I I T S L T G R D K N Q V B G B V Q I V S CAGCAAACCAGAGGCCTCCTGGGATGCATTATCACAAGCCTCACCGGAAGGGATAAGAATCAGGTCGAGGGAGAGGTCCAGATTGTGTCC Gene : HepCla Segment# : 71 Offset : 1051 1st Codon : 1 G R D K N Q V E G B V Q I V S T A A Q T P L A T C I N G V C GGCAGAGACAAAAACCAAGTGGAAGGGGAAGTGCAAATCGTCAGCACAGCCGCTCAGACATTCCTCGCCACATGCATTAACGGAGTGTGT Gene : HepCla Segment# : 72 Offset : 1066 1st Codon : 1 TAAQTFLATCING V C W T V Y H G A G T R T I A S P ACCECTECCCAAACCTTTCTEGCTACCTGTATCAATEGCGTCTEGTEGGACCGTCTACCATEGCGCTGGCACAAGGACAATCGCTAGCCCT : HepCla Segment# : 73 : 1081 Offset 1st Codon : 1 W T V Y H G A G T R T I A S P K G P V I Q M Y T N V D Q D L TGGACAGTGTATCACGGAGCCGGAACCAGACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTACACAAACGTCGACCAAGACCTC Gene : HepCla Segment# : 74 Offset : 1096 1st Codon : 1 K G P V I Q M Y T N V D Q D L V G W P A P Q G S R S L T P C AAGGGACCCGTCATCCAAATGTATACCAATGTGGATCAGGATCTGGTCGGCTGGCCCGCTCCCAAGGCTCCAGGTCCCTGACACCCTGT

PCT/AU01/00622 WO 01/090197

118/216 Gene : HepCla Segment# : 75 Offset : 1111 1st Codon : 1 V G W P A P Q G S R S L T P C T C G S S D L Y L V T R H A D GTGGGATGGCCTCCCGGGGAAGCAGAAGCCTCACCCCTTGCACATGCGGAAGCTCCGACCTCACCTCGTGACAAGGCATGCCGAT Gene : HepCla Segment# : 76 Offset : 1126 1st Codon : 1 T C G S S D L Y L V T R H A D V I P V R R G D S R G S L L ACCTGTGGCTCCAGCGATCTGTATCTGGTCACCAGACACGCTGACGTCATCCCTGTGAGAAGGAGAGAGGCGATAGCAGAGGCTCCCTGCTC Segment# : 77 Offset : 1141 1st Codon : 1 VIPVRRRGDSRGSLLSPRPISYLKGSSGGP Gene : HepCla Segment# : 78 Offset : 1156 S P R P I S Y L K G S S G G P L L C P A G H A V G I P R A A AGCCCTAGGCCTATCTCCTACCTCAAGGGAAGCTCCGGCGGACCCCTCCTGTGTCCCGCTGGCCATGCCGCTCTGCAGTTTTCAGAGCCGCT Gene : HepCla Segment# : 79 : 1171 Offset 1st Codon : 1 L L C P A G H A V G I P R A A V C T R G V A K A V D P I P V Gene : HepCla Segment# : 80 Offset : 1186 1st Codon : 1 V C T R G V A K A V D F I P V E N L E T T M R S P V F T D N GTGTGTACCAGAGGCGTCGCCAAAGCCGTCGACTTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAAT : HepCla Segment# : 81 Offset : 1201 1st Codon : 1 ENLETTMRSPVFTDNSSPPAVPQSFQVAHL GAGAATCTGGAAACCACAATGAGAAGCCCTGTGTTTACCGATAACTCCAGCCCTCCCGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTC Gene : HepCla Segment# : 82 Offset S S P P A V P Q S F Q V A H L H A P T G S G K S T K V P A A Gene : HepCla Segment# : 83 Offset : 1231 1st Codon : 1 HAPTGSGKSTKVPAAYAAQGYKVLVLNPSV Gene : НерСlа Segment# : 84 Offset : 1246 1st Codon : 1 YAAQGYKVLVLNPSVAATLGPGAYMSKAHG TACGCTGCCCAAGGCTATAAGGTCCTGGAATCCCTCCGTGGCTGCCACACTGGGATTCGGAGCCTATATGTCCAAGGCTCACGGA

Gene : HepCla Segment# : 85

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1st Codon : 1 AATLGPGAYMSKAHGIDPNIRTGVRTITTG GCCGCTACCCTCGGCTTTGGCGCTTACATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGA Gene : HepCla Segment# : 86 Offset : 1276 1st Codon : 1 I D P N I R T G V R T I T T G S P I T Y S T Y G K F L A D G ATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATACGGAAAGTTTCTGGCTGACGGA : HepCla Segment# : 87 : 1291 1st Codon : 1 S P I T Y S T Y G K F L A D G G C S G G A Y D I I I C D E C AGCCCTATCACATACTCCACCTATGGCAAATTCCTCGCCGATGGCGGATGCTCCGGCGGAGCCTATGACATTATCATTTGCGATGAGTGT Gene : HepCla Segment# : 88 Offset : 1306 1st Codon : 1 G C S G G A Y D I I I C D E C H S T D A T S I L G I G T V L GECTGTAGCGGAGGCGCTTACGATATCATTATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGGCATTGGCACAGTGCTC Gene : HepCla Segment# : 89 Offset : 1321 1st Codon : 1 H S T D A T S I L G I G T V L D Q A E T A G A R L V V L A T CACTCCACCGATGCCACAAGCATTCTGGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTGCTCGCCACA Gene : HepCla Segment# : 90 Offset : 1336 1st Codon : 1 DQAETAGARLVVLATATPPGSVTVPHPNIE GACCAAGCCGAAACCGCTGGCGCTAGGCTCGTGGTCCTGGCTACCGCTACCCCTCCCGGAAGCGTCACCGTCCCCCATCCCAATATCGAA : HepCla Segment# : 91 Offset : 1351 1st Codon : 1 A T P P G S V T V P H P N I B B V A L S T T G B I P F Y G K GCCACACCCCTGGCTCCGTGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAA Gene : HepCla Segment# : 92 Offset : 1366 1st Codon : 1 BVALSTTGEIPFYGKAIPLEVIKGGR_HLI_F GAGGTOGCCCTCAGCACAACCGGAGAGATTCCCTTTTACGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGACACCTCATCTTT Gene : HepCla Segment# : 93 Offset : 1381 1st Codon : 1 A I P L B V I K G G R H L I F C H S K K K C D E L A A K L V GCCATTCCCCTCGAGGTCATCAAAGGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAAGTGTGACGAACTGGCTGCCAAACTGGTC Gene : HepCla Segment# : 94 Offset : 1396 C H S K K K C D B L A A K L V A L G I N A V A Y Y R G L D V TGCCATAGCAAAAAGAAATGCGATGAGCTCGCCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCTCGACGTC Gene : HepCla Segment# : 95 Offset : 1411 1st Codon : 1 ALGINAVAYYRGLDVSVIPTSGDVVVATD GCCCTCGGCATTAACGCTGTGGCTTACTATAGGGGACTGGATGTGTCCCGTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGAT

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: HepCla Segment# : 96 Offset : 1426 1st Codon : 1 SVIPTSGDVVVVATDALMTGYTGDPDSVID AGGGTCATCCCTACCTCCGGCGATGTGGTCGTCGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGATTTCGATAGCGTCATCGAT : HepCla Segment# : 97 Offset : 1441 1st Codon : 1 A L M T G Y T G D F D S V I D C N T C V T Q T V D F S L D P GCCCTCATGACAGGCTATACCGGAGACTTTGACTCCGTGATTGACTGTAACACATGCGTCACCCAAACCGTCGACTTTAGCCTCGACCCT Gene : HepCla Segment# : 98 Offset : 1456 1st Codon: 1
CNTCVTQTVDFSLDPTFTIETTTLPQDAVS TGCANTACCTGTGTGACACAGACAGTGGATTTCTCCCTGGATCCCACATTCACAATCGAAACCACAACCCTCCCCCAAGACGCTGTGTCC Gene : HepCla Segment# : 99 Offset : 1471 1st Codon : 1 T F T I B T T T L P Q D A V S R T Q R R G R T G R G K P G I ACCTTTACCATTGAGACAACCACACTGCCTCAGGATGCCGTCAGCAGAACCCAAAGGAGAGGCAGAACCGGAAGGGGAAAGCCTGGCATT Gene : HepCla Segment# : 100 Offset : 1486 RT Q R R G R T G R G K P G I Y R P V A P G E R P S G M F D AGGACACAGAGAAGGGGAAGGCAGGCAGACCCAGACCCGGAATCTATAGGTTTGTGGCTCCCGGAGAGACCCTCCGGCATGTTCGAT : HepCla Segment# : 101 : 1501 Offset 1st Codon: 1
YRFVAPGBRPSGMFDSSVLCBCYDAGCAWY TACAGATTCGTCGCCCCTGGCGAAAGGCCTAGCGGAATGTTTGACTCCAGCGTCCTGTGAGTGTTACGATGCCGGATGCGCTTGGTAT : HepCla Segment# : 102 : 1516 1st Codon : 1 SSVLCBCYDAGCAWYELTPAETTVRLRAYM AGCTCCGTGCTCTGCGAATGCTATGACGCTGGCTGTGCCTGGTACGAACTGACACCCGCTGAGACAACCGTCAGGCTCAGGGCTTACATG Gene : HepCla Segment# : 103 : 1531 BLTPARTTVRLRAYMNTPGLPVCQDHLEFW GAGCTCACCCCTGCCGAAACCACAGTGAGACTGAGAGCCTATATGAATACCCCTGGCCTCCCCGTCTGCCAAGACCATCTGGAATTCTGG Gene : HepCla Segment# : 104 : 1546 1st Codon : 1 NTPGLPVCQDHLBFWEGVFTGLTHIDAHFL AACACCCCGGACTGCCTGTGTCAGGATCACCTCGAGTTTTGGGAAGGCGTCTTCACAGGCCTCACCCATATCGATGCCCATTTCCTC : HepCla Gene Segment# : 105 Offset : 1561 1st Codon : 1 B G V F T G L T H I D A H F L S Q T K Q S G E N F P Y L V A

Gene : HepCla Segment# : 106

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Offset : 1576 1st Codon : 1 S Q T K Q S G E N F P Y L V A Y Q A T V C A R A Q A P P P S AGCCAAACCAAACAGTCCGGCGAAAACTTTCCCTATCTGGTCGCCTATCAGGCTACCGTCTGCGCTAGGGCTCCAGGCTCCCCCTCC Gene : HepCla Segment# : 107 Offset : 1591 1st Codon : 1 YQATVCARAQAPPPSWDQMWKCLIRLKPTL TACCAAGCCACAGTGTGTGCCAGAGCCCCAAGCCCCTCCCCCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTC Gene : HepCla Segment# : 108 Offset : 1606 1st Codon : 1 W D Q M W K C L I R L K P T L H G P T P L L Y R L G A V O N TGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTACCCCTCTGCTCTACAGACTGGGAGCCGTCCAGAAT Gene : HepCla Segment# : 109 Offset : 1621 H G P T P L L Y R L G A V Q N E V T L T H P V T K Y I M T C Gene : HepCla Segment# : 110 Offset : 1636 1st Codon : 1 EVTLTHPVTKYIMTCMSADLEVVTSTWVLV Gene : HepCla Segment# : 111 Offset : 1651 1st Codon : 1 M S A D L B V V T S T W V L V G G V L A A L A A Y C L S T G Gene : HepCla Segment# : 112 Offset : 1666 1st Codon : 1 G G V L A A L A A Y C L S T G C V V I V G R I V L S G K P A GGCGGAGTGCTCGCCGCTCTGGCTGCCTATTGCCTCAGCACAGGCTGTGGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCT Gene : HepCla Segment# : 113 : 1681 Offset C V V I V G R I V L S G K P A I I P D R E V L Y R E F D E M TECETCETGATTGTGGGAAGGATTGTGCTCAGCGGAAAGCCTGCCATTATCCCTGACAGAGGGTCCTGTATAGGGAATTCGATGAGATG Gene : HepCla Segment# : 114 Offset : 1696 1st Codon : 1 I I P D R B V L Y R E P D B M B B C S Q H L P Y I B Q G M M ATCATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAGAGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATG : HepCla Gene Segment# : 115 Offset : 1711 1st Codon : 1 EECSQHLPYIEQGMMLAEQFKQKALGLLQT GAGGAATGCTCCCAGCATCTGCCTTACATTGAGCAAGGCATGATGCTCGCCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACA Gene : HepCla Segment# : 116 Offset : 1726 1st Codon : 1

Figure 26 (Cont)

L A E Q F K Q K A L G L L Q T A S R Q A E V I A P A V Q T N

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CTGGCTGAGCAATTCAAACAGAAAGCCCTCGGCCTCCTGCAAACCGCTAGCAGACAGGCTGAGGTCATCGCTCCCGCTGTGCAAACCAAT Gene : HepCla

Gene : HepCla Segment# : 117 Offset : 1741 1st Codon : 1

A S R Q A E V I A P A V Q T N W Q K L E V F W A K H M W N F GCCTCCAGGCAAGCCGAAGTGATTGCCCCTGCCGTCCAGACAAACTGGCAGACTGTTTTTGGGCTAAGCATATGTGGAACTTT

Gene : HepCla Segment# : 118 Offset : 1756 1st Codon : 1

W Q K L E V F W A K H M W N F I S G I Q Y L A G L S T L P G TGGCAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTTCATTAGCGGAATCCAATACCTCGCCGGACTGTCCACCCTCCCCGGA

Gene : HepCla Segment# : 119 Offset : 1771 1st Codon : 1

Gene : HepCla Segment# : 120 Offset : 1786 1st Codon : 1

N P A I A S L M A F T A A V T S P L T T S Q T L L F N I L G AACCCTGCCATTGCCTCCTGATGGCCTTTACCGCTGCCGTCACCTCCCCCTCACCACAACCCTCCTGTTTAACATTCTGGGA

Gene : HepCla Segment# : 121 Offset : 1801 1st Codon : 1

S P L T T S Q T L L F N I L G G W V A A Q L A A P G A A T A AGCCCTCTGACAACCTCCCAGACACCTCTCAATATCCTCGGGGATGGGTCGCCGCTCAGCTCGCCGCTCCCGGAGCCGCTACCGCT

Gene : HepCla Segment# : 122 Offset : 1816 1st Codon : 1

Gene : HepCla Segment# : 123 Offset : 1831 1st Codon : 1

PVGAGLAGAAIGSVGLGKVLVDILAGYGAGCCCCGATACCGCAGAGCCCCCGAAAGTCCTCCGCCGATACCGCAGACCCCCGA

Gene : HepCla Segment# : 124 Offset : 1846 1st Codon : 1

L G K V L V D I L A G Y G A G V A G A L V A F K I M S G B V CTGGGAAAGGTCCTGGCGTCGACATTCTGGCTGGCTATGGCGCTGGCGTCGCCGGAGCCCTCGTGGCTTTCAAAATCATGAGCGGAGAGGTC

Gene : HepCla Segment# : 125 Offset : 1861 1st Codon : 1

Gene : HepCla Segment# : 126 Offset : 1876 1st Codon : 1

PSTBDLVNLLPAILSPGALVVGVCAAILRCCCCCCGAAGACCTCGTGCATCTGCACCGAAGACCTCGTGAATCTGCTCCCCGCTATCCTCAGCCCTGGCGCTCTGGTGGGAGTGGTCTGCGCTGCCCATTCTGAGA

Gene : HepCla

123/216 Segment# : 127 Offset : 1891 1st Codon: 1 PGALVVGVVCAAILRRHVGPGBGAVQWMNR CCCGGAGCCCTCGTCGTCGCCGTGTGTGTCCCCCTATCCTCAGGAGACACGTCGGCCCTGGCGAAGGCGCTGTGCAATGGATGAACAGA : HepCla Segment# : 128 Offset : 1906 R H V G P G B G A V Q W M N R L I A F A S R G N H V S P T H AGGCATGTGGGACCCGGAGAGGGGAGCCGTCCAGTGGATGAATAGGCTCATCGCTTTCGCTAGCAGAGGCAATCACGTCAGCCCTACCCAT Gene : HepCla Segment# : 129 Offset : 1921 1st Codon : 1 LIAFASRGNHVSPTHYVPESDAAARVTAIL CTGATTGCCTTTGCCTCCAGGGGAAACCATGTGTCCCCCACACACTATGTGCCTGAGTCCGACGCTGCCGCTAGGGTCACCGCTATCCTC : HepCla Gene Segment# : 130 Offset : 1936 1st Codon : 1 Y V P E S D A A A R V T A I L S S L T V T Q L L R R L H Q W TACGTCCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCCAACTGCTCAGGAGACTGCATCAGTGG : НерС1а Gene Segment# : 131 Offset : 1951 1st Codon: 1
S S L T V T Q L L R R L H Q W I S S E C T T P C S G S W L R : HepCla Segment# : 132 Offset 1st Codon : 1 I S S E C T T P C S G S W L R D I W D W I C E V L S D P K T ATCTCCAGCGAATGCACAACCCCTTGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGGATCTGTGAGGTCCTGTCCAGCTTTAAGACA Gene : HepCla Segment# : 133 Offset : 1981 1st Codon : 1 DIWDWICEVLS DFKTWLKAKLMPQLPGIPF GACATTTGGGATTGGATTTGCGAAGTGCTCAGCGATTTCAAAACCTGGCTGAAAGCCAAACTGATGCCCCAACTGCCTTGCCTTTT Gene : HepCla Segment# : 134 Offset : 1996 1st Codon : 1 W L K A K L M P Q L P G I P F V S C Q R G Y K G V W R G D G TGGCTCAAGGCTAAGCTCATGCCTCAGCTCCCCGGAATCCCTTTCGTCAGCTGTCAGAGAGGCTATAAGGGAGTGTGGAGGGGAGACGGA Gene : HepCla Segment# : 135 Offset : 2011 V S C Q R G Y K G V W R G D G I M H T R C H C G A B I T G H

GTGTCCTGCCAAAGGGGATACAAAGGCGTCTGGAGAGGCGATGGCATTATGCATACCAGATGCCATTGCGGAGCCGAAATCACAGGCCAT

Gene : HepCla Segment# : 136 Offset : 2026 1st Codon : 1

I M H T R C H C G A B I T G H V K N G T M R I V G P R T C R ATCATGCACACAAGGTGTCACTGTGGCGCTGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGA

Gene : HepCla Segment# : 137 Offset : 2041 1st Codon : 1

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V K N G T M R I V G P R T C R N M W S G T P P I N A Y T T G
 : HepCla
 Segment# : 138
 Offset
       : 2056
1st Codon : 1
 N M W S G T P P I N A Y T T G P C T P L P A P N Y T P A L W
AACATGTGGTCCGGCACATTCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCTCCCCGCTCCCCAATTACACATTCGCTCTGTGG
Gene
       : HepCla
Segment# : 139
Offset
       : 2071
1st Codon : 1
 PCTPLPAPNYTFALWRVSABEYVEIRRVGD
CCCTGTACCCCTCTGCCTGCCCCTAACTATACCTTTGCCCTCTGGAGAGTGTCCGCCGAAGAGTATGTGGAAATCAGAAGGGTCGGCGAT
       : HepCla
Gene
Segment# : 140
Offset
       : 2086
1st Codon : 1
 R V S A E E Y V E I R R V G D F H Y V T G M T T D N L K C P
AGGGTCAGCGCTGAGGAATACGTCGAGATTAGGAGAGTGGGAGACTTTCACTATGTGACAGGCATGACCACAGACAATCTGAAATGCCCT
       : HepCla
Segment# : 141
Offset
       : 2101
1st Codon : 1
 PHYVTG M T T D N L K C P C Q V P S P E P F T E L D G V
TTCCATTACGTCACCGGAATGACAACCGATAACCTCAAGTGTCCCTGTCAGGTCCCCTCCCCGGAATTCTTTACCGGACTGGATGGCGTC
Gene
       : HepCla
Segment# : 142
Offset
       : 2116
1st Codon : 1
 C Q V P S P E F F T E L D G V R L H R F A P P C K P L L R E
Gene
       : HepCla
Segment# : 143
Offset
       : 2131
1st Codon : 1
RLHRFAPPCKPLLREBVSFRVGLHBYPVGS
AGGCTCCACAGATTCGCTCCCCTTGCAAACCCCTCCTGAGAGAGGGAAGTGTCCTTCAGAGTGGGGACTGCATGAGTATCCCGTCGGCTCC
       : HepCla
Gene
Segment# : 144
Offset
      : 2146
1st Codon: 1
EVSFRVGLHEYPVGSQLPCEPEPDVAVLTS
GAGGTCAGCTTTAGGGTCGGCCTCCACGAATACCCTGTGGGAAGCCAACTGCCTTGCGAACCCGAACCCGATGTGCTCACCTCC
       : HepCla
Segment# : 145
Offset
      : 2161
lst Codon: 1
Q L P C E P E P D V A V L T S M L T D P S H I T A E A A G R
CAGCTCCCCTGTGAGCCTGAGCTCGCCGTCCTGACAAGCATCGCCGAAGCCCTAGCCATATCACAGCCGAAGCCGCTGGCAGA
       : HepCla
Segment# : 146
Offset
      : 2176
1st Codon : 1
M L T D P S H I T A B A A G R R L A R G S P P S M A S S S A
: HepCla
Segment# : 147
Offset
      : 2191
1st Codon : 1
RLARGSPPSMASSSASQLSAPSLKATCTA
AGGCTCGCCAGAGGCTCCCCCCTAGCATGGCCTCCAGCTCCCGCCTCCCCGCAGCCCCCCTGAAAGCCACATGCACAGCCAAT
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Gene : HepCla Segment# : 148 Offset : 2206 1st Codon : 1

SQLSAPSLKATCTANHDSPDABLIEANLLW
AGCCAACTGTCCGCCCCAACCTGACCCCCAACCTGACCCCCCAACTGATTGAGGCTAACCTCCTGTGG

Gene : HepCla Segment# : 149 Offset : 2221 1st Codon : 1

H D S P D A E L I E A N L L W R Q E M G G N I T R V E S E N CACGATAGCCCTGAGGCTCATCGAAGCCCAATCTGCTCTGGAGACAGGAAATGGGAGGCCAATATCACAAGGGTCGAGTCCGAGAAT

Gene : HepCla Segment# : 150 Offset : 2236 1st Codon : 1

RQBMGGNITRVESENKVVILDSPDPLVA E B AGGCAAGAGATGGCGGAAACATTACCAGGTGGAAAGCGAAAACAAGTGGTCATCCTCGACTCCTTCGATCCCTCGTGGCTGAGGAA

Gene : HepCla Segment# : 151 Offset : 2251 1st Codon : 1

K V V I L D S F D P L V A E E D E R E I S V P A E I L R K S AAGGTCGTGATTCTGGATAGCTTCTGAGAAAGTCC

Gene : HepCla Segment# : 152 Offset : 2266 lst Codon : 1

DEREISVPAEILRKSRFAQALPVWARPDY GACGAAAGGGAAATCTCCGTGCCTGCCGAAATCTCAGGAAAAGCAGAAGGTTTGCCCAAGCCCTCCCGTCTGGGCTAGGCCTGACTAT

Gene : HepCla Segment# : 153 Offset : 2281 1st Codon : 1

R R F A Q A L P V W A R P D Y N P P L V B T W K K P D Y E P AGGAGATTCGCTCAGGCTCTGCCTGTGGGCCAGACCCGATTACAATCCCCCTCTGGTCGAGACATGGAAAAAGCCTGACTATGAGCCT

Gene : HepCla Segment# : 154 Offset : 2296 1st Codon : 1

Gene : HepCla Segment# : 155 Offset : 2311 1st Codon : 1

Gene : HepCla Segment# : 156 Offset : 2326 1st Codon : 1

V P P P R K K R T V V L T E S T L S T A L A E L A T K S P G GTGCCTCCCCCTAGGAAAAGAACCGTCGTCCTCCCAAAAGTCCTTCGGA

Gene : HepCla Segment# : 157 Offset : 2341 1st Codon : 1

T L S T A L A E L A T K S P G S S S T S G I T G D N T T T S ACCCTCAGCACAGCCCTCGCCGAACTGCCTACCAAAAGCTTTGGCTCCAGCTCCACCTCCGGCATTACCGGAGACAATACCACAAACCTCC

Gene : HepCla Segment# : 158 Offset : 2356

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1st Codon : 1 S S S T S G I T G D N T T T S S B P A P S G C P P D S D A E AGCTCCAGCACAAGCGGAATCACAGGCGATAACACAACCACAAGCTCCGAGCCTGCCCCTAGCGGATGCCCTCCCGATAGCGATGCCGAA : HepCla Segment# : 159 Offset : 2371 1st Codon : 1 SEPAPSGC'PPDSDAESYSSMPPLEGEPGDP AGGGAACCGGTCCCTCGGCTGTCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGGGGAACCCGGAGACCCT Gene : HepCla Segment# : 160 Offset : 2386 1st Codon : 1 S Y S S M P P L B G B P G D P D L S D G S W S T V S S E A G AGCTATAGCTCCATGCCTCCCTCGAGGGGGGGGGGGCTCGCGATCCCGATCTGTCCGACGGAGCTGGAGCACAGTGTCCAGCGAAGCCGGA Gene : KepCla Segment# : 161 Offset : 2401 1st Codon : 1 D L S D G S W S T V S S E A G T E D V V C C S M S Y S W T G GACCTCAGCGATGGCTCCTGGTCCACCGTCAGCTCCGAGGCTGGCACAGAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGGA : HepCla Segment# : 162 Offset : 2416 1st Codon : 1 TEDVVCCSMSYSWTGALVTPCAAEEQKLPI ACCGAAGACGTCGTGTGTTGCTCCATGTCCTACTCCTGGACAGGCGCTCTGGTCACCCCTTGCGCTGACGCGAAAGGCTACACCCCATT : HepCla Segment# : 163 : 2431 1st Codon : 1 A L V T P C A A E B Q K L P I N A L S N S L L R H H N L V Y GCCCTCGTGACACCCTGTGCCGCTGAGGAACAGAAACTGCCTATCAATGCCCTCAGCAATAGCCTCCTGAGACACCATAACCTCGTGTAT Gene : HepCla Segment# : 164 Offset : 2446 1st Codon : 1 N A L S N S L L R H H N L V Y S T T S R S A C Q R Q K K V T Gene : HepCla Segment# : 165 Offset : 2461 1st Codon : 1 S T T S R S A C Q R Q K K V T F D R L Q V L D S H Y O D V L AGCACAACCTCCAGGTCCGCCTGTCAGAGACAGAAAAAGGTCACCTTTGACAGACTGCAAGTGCTCGACTCCCACTATCAGGATGTGCTC Gene : HepCla Segment# : 166 Offset : 2476 1st Codon : 1 PDRLQVLDSHYQDVLKBVKAAASKV_{KANL}L TTCGATAGGCTCCAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAGAGGTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTC Gene : HepCla Segment# : 167 : 2491 Offset 1st Codon : 1 K B V K A A A S K V K A N L L S V B E A C S L T P P H S A K AAGGAAGTGAAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCTGTCCGTGGAAGAGGCTTGCTCCCTGACACCCCCTCACTCCGCCAAA Gene : HepCla Segment# : 168 : 2506 Offset S V B B A C S L T P P H S A K S K F G Y G A K D V R C H A R AGCSTCGAGGAAGCCTGTAGCCTCACCCCTCCCCATAGCGCTAAGTCCAAGTTTGGCTATGGCGAAGGATGTGAGATGCCATGCCAGA

PCT/AU01/00622 WO 01/090197

127/216 : HepCla Gene Segment# : 169 Offset : 2521 1st Codon : 1 SKFGYGAKD V R C H A R K A V A H I N S V W K D L L E AGCAAATTCGGATACGGAGCCAAAGACGTCAGGTGTCACGCTAGGAAAGCCGTCGCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAA Gene : HepCla Segment# : 170 Offset : 2536 1st Codon : 1 K A V A H I N S V W K D L L E D S V T P I D T T I M A K N E AAGGCTGTGGCTCACATTAACTCCGTGTGGAAGGATCTGCTCGAGGATAGCGTCACCCCTATCGATACCACAATCATCGCCAAAAACGAA Gene : HepCla Segment# : 171 : 2551 Offset DSVTPIDTTIMAKNBVFCVQPBKGGRKPA GACTCCTGACACCCATTGACACCACTATGGCTAAGAATGAGGTCTTCTGTGCAACCCGAAAAGGGGAGGCAGAAAGCCTGCCAGA Gene : HepCla Segment# : 172 Offset : 2566 1st Codon : 1 V P C V Q P B K G G R K P A R L I V P P D L G V R V C B K M GTGTTTTGCGTCCAGCCTGAGAAAGGCGGAAGGAAACCCGCTAGGCTCATCGTCTTCCCTGACCTCGGCGTCAGGGTCTGCGAAAAGATG : HepCla Gene Segment# : 173 Offset : 2581 1st Codon : 1 LIVFPDLGVRVCBKMALYDVVSKLPLAVMG CTGATTGTGTTTCCCGATCTGGGAGTGAGAGTGTGTGAGAAAATGGCTCTGTATGACGTCGTGTCCAAGCTCCCCCTCGCCGTCATGGGA : HepCla Segment# : 174 Offset : 2596 1st Codon : 1 A L Y D V V S K L P L A V M G S S Y G P Q Y S P G Q R V E F GCCCTCTACGATGTGGTCAGCAAACTGCCTCTGGCTGTGATGGCTCCAGCTATGGCTTTCAGTATAGCCCTGGCCAAACGGTCGAGTTT Gene : HepCla
Segment# : 175 : 2611 Offset 1st Codon : 1 S S Y G F Q Y S P G Q R V B F L V Q A W K S K K T P M G F S AGCTCCTACGGATTCCAATACTCCCCCGGACAGAGAGTGGAATTCCTCGTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGGATTCTCC Gene : HepCla Segment# : 176 Offset : 2626 LVQAWKSKKTPMGFSYDTRCFDSTVTBSDI CTGGTCCAGGCTTGGAAAAGCAAAAAGACACCCATGGGCTTTAGCTATGACACAAGGTGTTTCGATAGCACAGTGACAGAGTCCGACATT Gene : HepCla Segment# : 177 Offset : 2641 1st Codon : 1 Y D T R C F D S T V T E S D I R T E E A I Y Q C C D L D P Q

Gene : HepCla Segment# : 178 Offset : 2656

R T B B A I Y Q C C D L D P Q A R V A I K S L T E R L Y V G AGGACAGAGGCATTTACCAATGCTGTGACCTCGACCCTCAGGCTAGGGTCGCCATTAAGTCCCTGACAGAGACACTGTATGTGGGA

Gene : HepCla Segment# : 179

128/216 Offset : 2671 1st Codon : 1 A R V A I K S L T B R L Y V G G P L T N S R G B N C G Y R R GCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGACCCCTCACCAATAGCAGAGGCGAAAACTGTGGCTATAGGAGA Gene : HepCla Segment# : 180 Offset : 2686 1st Codon : 1 G P L T N S R G B N C G Y R R C R A S G V L T T S C G N T L GGCCCTCTGACAAACTCCAGGGGAGAGAATTGCGGATACAGAAGGTGTAGGGGCTAGCGGAGTGCTCACCACAAGCTGTGGCAATACCCTC Gene : HepCla Segment# : 181 Offset : 2701 1st Codon : 1 C R A S G V L T T S C G N T L T C Y I K A R A A C R A A G L TGCAGAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAAAGCCAGAGCCGCTTGCAGAGCCGCTGGCCTC Gene : HepCla Segment# : 182 Offset : 2716 1st Codon : 1 T C Y I K A R A A C R A A G L Q D C T M L V C G D D L V V I ACCTGTTACATTAAGGCTAGGGCTGCCTGTAGGGCTGCCGGACTGCAAGACTGTACCATGCTGGTCTGGGAGACGATCTGGTCGTGATT : HepCla Segment# : 183 Offset : 2731 1st Codon : 1 Q D C T M L V C G D D L V V I C B S A G V Q B D A A S L R A CAGGATTGCACAATGCTCGTGTGTGGCGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCGCTAGCCTCAGGGCT Gene : HepCla Segment# : 184 : 2746 1st Codon : 1 C E S A G V Q B D A A S L R A F T E A M T R Y S A P P G D P TGCGAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGAGAGCCTTTACCGAAGCCATGACCAGATACTCCGCCCCTCCCGGAGACCCT Gene : HepCla Segment# : 185 Offset : 2761 F T E A M T R Y S A P P G D P P Q P R Y D L E L I T S C S S TTCACAGAGGCTATGACAAGGTATAGCGCTCCCCTTGGCGATCCCCCTCAGCCTGAGTATGACCTCGAGCTCATCACAAGCTGTAGCTCC Gene : HepCla Segment# : 186 Offset : 2776 1st Codon : 1 P Q P E Y D L E L I T S C S S N V S V A H D G A G K R V Y Y CCCCAACCCGAATACGATCTGGAACTGATTACCTCCTGCTCCAGCAATGTGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTAT Gene : HepCla Segment# : 187 Offset : 2791 1st Codon : 1 N V S V A H D G A G K R V Y Y L T R D P T T P L A R A A N B AACGTCAGCGTCGCCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCTACCACACCCCTCGCCAGAGCCGCTTGGGAA : HepCla Gene Segment# : 188 Offset : 2806 1st Codon : 1 LTRDPTTPLARANETARHTPVNSWLGNII CTGACAAGGGATCCCACAACCCCTCTGGCTAGGGCTGCCTGGGAGACAGCCAGACACCCCGTCAACTCCTGGCTCGGCAATATCATT Gene : HepCla Segment# : 189 Offset : 2821

Figure 26 (Cont)

TARHTP V N S W L G N I I M F A P T L W A R M I L M T H

1st Codon : 1

PCT/AU01/00622 WO 01/090197

129/216 ACCECTAGGCATACCCCTGTGAATAGCTGGCTGGGAAACATTATCATGTTCGCTCCCACACTGTGGGCCAGAATGATTCTGATGACCCAT Gene : HepCla Segment# : 190 Offset : 2836 1st Codon : 1 M P A P T L W A R M I L M T H P P S V L I A R D Q L E Q A L ATGTTTGCCCCTACCCTCTGGGCTAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAAGCCCTC : HepCla Segment# : 191 Offset : 2851 FFSVLIARDQLBQALDCBIYGACYSIEPLD TTCTTTAGCGTCCTGATTGCCAGAGCCAACTGGAACAGGCTCTGGATTGCGAAATCTATGGCGCTTGCTATAGCATTGAGCCTCTGGAT : HepCla Segment# : 192 Offset : 2866 1st Codon : 1 D C E I Y G A C Y S I E P L D L P P I I Q R L H G L S A F S GACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCTATCATTCAGAGACTGCATGGCCTCAGCGCTTTCTCC : HepCla Segment# : 193 : 2881 Offset 1st Codon : 1 L P P I I Q R L H G L S A F S L H S Y S P G E I N R V A A C CTGCCTCCCATTATCCAAAGGCTCCACGGACTGTCCGCCTTTAGCCTCCACTCCTACTCCCCGGGAGAGATTAACAGAGTGGCTGCCTGT Gene : HepCla Segment# : 194 Offset : 2896 1st Codon : 1 L H S Y S P G E I N R V A A C L R K L G V P P L R A W R H R CTGCATAGCTATAGCCCTGGCGAAATCAATAGGGTCGCCGCTTGCCTCAGGAAACTGGGAGTGCCTCCCCTCAGGGCTTGGAGACACAGA Gene : RepCla Segment# : 195 Offset : 2911 1st Codon : 1 L R K L G V P P L R A W R H R A R S V R A R L L A R G G R A CTGAGAAAGCTCGCCGTCCCCCTCTGAGAGCCTGGAGGCATAGGGCTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGGCGGAAGGGCT : HepCla Segment# : 196 Offset : 2926 1st Codon : 1 ARS V RARLLARG G RAAICG KYLFN WAVRTK GCCAGAAGCGTCAGGGCTAGGCTCCTGGCTAGGGGAGGCAGAGCCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAA : HepCla Gene Segment# : 197 : 2941 1st Codon : 1 A I C G K Y L F N W A V R T K L K L T P I A A A G R L D L S GCCATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGACTGGATCTGTCC Gene : HepCla Segment# : 198 : 2956

1st Codon : 1

LKLTPIAAAGRLDLSGWFTAGYSGGDIYHS

Gene : HepCla Segment# : 199 1st Codon : 1

G W F T A G Y S G G D I Y H S V S H A R P R W F W P C L L L GGCTGGTTCACAGCCGGATACTCCGGCGGAGACATTTACCATAGCGTCAGCCATGCCAGACCCAGATGGTTTTGGTTTTTGCCTCCTGCTC

Gene : HepCla

130/216

Segment# : 200 Offset : 2986 1st Codon : 1

V S H A R P R W F W F C L L L L A A G V G I Y L L P N R A A GTGTCCCACGCTAGGTGGTTCTGGTTCTGGTCTGCTCGCCGCGCGTTGGCGTTTACCTCCTGCCTAACAGAGCCGCT

Gene : HepCla Segment# : 201 Offset : 3001 1st Codon : 1

L A A G V G I Y L L P N R A A CTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCC

Segments in scrambled order:

HepCla #77

V I P V R R R G D S R G S L L S P R P I S Y L K G S S G G P GTGATTCCCGTCAGGGGAGGCCCCTTGTCCCCCAGACCCATTAGCTATCTGAAAGGCTCCAGGGGAGGCCCT

HepCla #68

ARRGREILLGPADGMVSKGWRLLAPITAYA

HepCla #143

R L H R F A P P C K P L L R B B V S F R V G L H B Y P V G S AGGCTCCACAGATTCCCCCCTTGCAAACCCCTCCTGAGAGGGAAGTGTCCTTCAGAGTGGACTGCATGAGTATCCCGTCGCTCC

HepCla #66

V V F S Q M E T K L I T W G A D T A A C G D I I N G L P V S GTGGTCTTCTCCCAGATGGAGACAAAGCTCATCACATGGGGAGCCGATACCGCTGCCTGTGCCGATATCATTAACGGACTGCCTGTGCC

HepCla #79

L L C P A G H A V G I F R A A V C T R G V A K A V D F I P V CTGCTCTGCCCTGCCCGACAGGGGACTGCTGTGGATTTCATTCCCGTC

HepCla #113

C V V I V G R I V L S G K P A I I P D R E V L Y R B F D E M
TGCGTCGTGATTGTGGGAAGGATTGTGCTCAGCGGAAAGCCTGCCATTATCCCTGACAGAGAGGGTCCTGTATAGGGAATTCGATGAGATG

HepCla #139

PCTPLPAPNYTFALWRVSAEEYVBIRRVGDCCCTGTACCCCTGCCCCTAACTATACCTTTGCCCTCTGGGGAGATGTCCGCCGAAGAGTATGTGGAAATCAGAAGGTCGGCGAT

HepCla #174

A L Y D V V S K L P L A V M G S S Y G F Q Y S P G Q R V B F GCCTCTACGATGTGGCTCAGCAAACGGTCGAGGTTT

HepCla #57

ISWCLWWLQYFLTRVBAQLHVWVPPLNVRG ATCTCCTGGTGTCTGGGGGCTCCAGTATTTCCTCACCAGGTGGAGCCCAACTGCATGTGGGTGCCTCCCCTCAACGTCAGGGGA

HepCla #51

ENLVILNAASLAGTHGLVSFLVFFCFAWYL

HepCla #193

LPPIIQRLHGLSAFSLHSYSPGBINRVAACCTGCCTCCCATTATCCAAAGGCTCCACGGACTGTCCGCCTTTAGCCTCCCACTCCTACTCCCCCGGAGAGATTAACAGAGTGGCTGCCTGT

HepCla #154

N P P L V E T W K K P D Y E P P V V H G C P L P P P R S P P AACCCTCCCCTGTGGAAACCTGGAAGAAACCCGATTACGAACCCCCTGTGGTCCACGGATGCCCTCTGCCTCCCCCTAGGTCCCCCCT

HepCla #48

G V G S S I A S W A I K W E Y V V L L F L L A D A R V C S GGGTCGGCTCCAGCATTGCCTCCTGGCTACGCTTACAATGGGAATACGTCGTGCTCCTGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCC

HenCla #37

L N N T R P P L G N W F G C T W M N S T G F T K V C G A P P CTGAATAACACAAGGCCTCCCCTCGGCAATTGGTTTGGCTGTTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCT

HepCla #185

F T E A M T R Y S A P P G D P P Q P E Y D L E L I T S C S S

131/216

TTCACAGAGGCTATGACAAGGTATAGCGCTCCCCTGGCGATCCCCCTCAGCCTGAGCTATGACCTCCAGCCTCATCACAAGCTGTAGCTCC

HepCla #54

HepCla #70

QQTRGLLGCIITSLTGRDKNQVEGEVQIVS CAGCAAACCAGAGGCCTCCTGGGATGCATTATCACAAGCCTCACCGGAAGGGATAAGAATCAGGTCGAGGGAGAGGTCCAGATTGTGTCC

HepCla #82

RepCla #104

N T P G L P V C Q D H L B F W B G V F T G L T H I D A H F L AACACACCCGGACTGCCTGTGTCAGGATCACCTCGAGTTTTCGCGAGGCGTCTTCACAGGCCTCACCCCATATCGATGCCCATTTCCTC

HepCla #26

HepCla #110

HepCla #56

HepCla #197

A I C G K Y L F N W A V R T K L K L T P I A A G R L D L S GCCATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCAGACTGGATCTGTCC

HepCla #25

I À Y F S M V G N W A K V L V V L L L F A G V D A E T H V T ATCECTTACTTAGCATGGTGGGAAACTGGGCCAAAGTGCTCGTGGTCCTGCTCCTGTTTGCCGGAGTGGATGCCGAAACCCATGTGACA

HepCla #147

HepCla #52

G L V S F L V F F C F A W Y L K G R W V P G A V Y A L Y G M GGCCTCGTGTCCTCCTCGTGTTTTCTGTTTCGCTTGGTATCTGAAAGGCAGATGGGTCCCCGGAGCCGTCTACGCTCTGTATGGCATG

HepCla #145

Q L P C B P E P D V A V L T S M L T D P S H I T A E A A G R CAGCTCCCCTGTGAGCCTGACCTGACCTGCCGTCGCGAGCCGTGCCAGACCCGTGCCAGACCCGTGCCAGACCCGAAGCCGCTGGCAGA

HepCla #171

D S V T P I D T T I M A K N E V P C V Q P E K G G R K P A R GACTCCGTGACACCCATTGACACCAACCATTATGGCTAAGAATGAGGTCTTCTGTGCAACCCGAAAAGGGAGGCAGAAAGCCTGCCAGA

HepCla #84

Y A A Q G Y K V L V L N P S V A A T L G F G A Y M S K A H G TACGCTGCCCAAGGCTATAAGGTCCTGAATCCCTCGTGGCTGCCACACTGGATTCGGAGCCTATATGTCCAAGGCTCACGGA

HepCla #14

HepCla #175

S S Y G F Q Y S P G Q R V B F L V Q A W K S K K T P M G F S AGCTCCTACGGATTCCAATACTCCCCCGGACAGAGAGTGGAATTCCTCCTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGGATTCTCC

HepCla #67

HepCla #148

S Q L S A P S L K A T C T A N H D S P D A E L I E A N L L W AGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTACCGCTAACCATGACTCCCCCGATGCCGAACTGATTGAGGCTAACCTCCTGTGG

132/216

HepCla #120

N P A I A S L M A F T A A V T S P L T T S Q T L L F N I L G. AACCCTGCCATTGCCTCACCACAAGCCAAACCCTCCTGTTTAACATTCTGGGA

HepCla #176

L V Q A W K S K K T P M G F S Y D T R C F D S T V T B S D I CTGGTCCAGGCTTGGAAAAGACACACCCATGGCTTTAGCTATGACACAAGGTGTTTCGATAGCACAGTGACAGAGTCCGACATT

HepCla #152

D B R B I S V P A R I L R K S R R F A Q A L P V W A R P D Y GACGAAAGGGAAATCTCCAGGAAATCTCAGGAAAAGCAGAAGGTTTGCCCAAGCCCTCCCGTCTGGGCTAGGCCTGACTAT

HepCla #190

M F A P T L W A R M I L M T H F F S V L I A R D Q L E Q A L ATGITTGCCCCTACCCTCTGGGCTAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAAGCCCTC

HepCla #96

S V I P T S G D V V V V A T D A L M T G Y T G D F D S V I D AGCGTCATCCCTACCTCCGCGGATGTGGTCGTCGTCGCCACAGACGCTCTGATGACCGGGATACACAGGCGGATTTCGATAGCGTCATCGAT

HepCla #94

CHSKKKCDBLAAKLVALGINAVAYYRGLDV TGCCATAGCAAAAAGAAATGCGATGGCTCGCCCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCTCGACGTC

HepCla #46

HepCla #53

K G R W V P G A V Y A L Y G M W P L L L L L A L P Q R A Y AAGGGAAGGTGGGTGCTGGGCTGTGTTATGCCCTCTACGGAATGTGGCCCCTCCTGCTCCTGGTCCTGGCTCTGCCTCAGAGAGCCCTAT

HepCla #87

S P I T Y S T Y G K F L A D G G C S G G A Y D I I I C D B C AGCCCTATCACATACTCCACCTATGGCAAATTCCTCGCCGATGGCGGATGCTCCGGCGGAGCCTATGACATTATCATTTGCGATGAGTGT

HepCla #196

ARSVRARLLARGGRAAICGKYLFNWAVRT K GCCAGAAGCGTCAGGGCTAGGGCTAGGGGAGGCCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAA

HepCla #170

KAVAHINSVWKDLLEDSVTPIDTTIMAKNB AAGGCTGTGGCTCACATTAACTCCGTGTGGAAGGATCTCGTGGGAAGACGAA AAGGCTGTGGCTCACATTAACTCCGTGTGGAAGGATCTCGTGGGCCAAAAACGAA

HepCla #35

F T P S P V V V G T T D R S G A P T Y S W G A N D T D V F V TTCACACCCTCCCCGTGGTGGTCGGCACAACCGATAGGTCCGGCGCTCCCACATACTCCTGGGGAGCCAATGACACAGACGTCTTCGTC

HepCla #16

PGCVPCVREGNASRCWVANTPTVATRDGKLCCCGGATGCCTCCCCTGTGTGAGAGGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCACAGTGGCTACCAGAGACGGAAAGCTC

HepCla #183

Q D C T M L V C G D D L V V I C E S A G V Q E D A A S L R A CAGGATTGCACAATGCTCGTGTGTGGCGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCGCTAGCCTCAGGGCT

HepCla #125

VAGALVAFKIMSGEVPSTEDLVNLLPAILS GTGGCTGGCGCTCTGGTCGCCTTTAAGATTATGTCCGGCGAAGTGCCTAGCACAGAGGATCTGGTCAACCTCCTGCCATTCTGTCC

HepCla #177

HepCla #103

ELTPAETTVRLRAYMNTPGLPVCQDHLEFWGGGCTCACCCCTGCCAAGACCACTCGGAATCTGG

HepCla #186

PQPBYDLBLITSCSSNVSVAHDGAGKRVYYCCCCAACCCGAATACGATCTGCAACACGATTACCTCCTCCTCCAGCAATGTCTCCTGCTCACGATGTCTCCTGCCAAAAGGGTCTACTAT

133/216

HepCla #9

LGKVIDTLTCGFADLMGYIPLVGAPLGGAA CTGGGAAAGGTCATCGATACCCTCACCTGTGGCTTTTGCCGATCTGATGGGCTATATCCCTCTGGTCGGCGCTCCCCTCGGCGGAGCCGCT

AIPLEVIKGGRHLIFCHSKKKCDELAAKLV GCCATTCCCCTCGAGGTCATCAAAGGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAAGTGTGACGAACTGGCTGACCAAACTGGTC

G G V L A A L A A Y C L S T G C V V I V G R I V L S G K P A ${\tt GGCGGAGTGCTCGGCTGCCTATTGCCTCAGCACAGGCTGTGTGGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCT}$

C B S A G V Q B D A A S L R A F T B A M T R Y S A P P G D P TGCGAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGAGAGGCCTTTACCGAAGCCATGACCAGATACTCCGCCCCTCCCGGAGACCCT

G W F T A G Y S G G D I Y H S V S H A R P R W F W F C L L L GGCTGGTTCACAGCCGGATACTCCGGCGGAGACATTTACCATAGCGTCAGCCAGACCCAGATGGTTTTGGTTTTGGCTCCTGCTC

S S S T S G I T G D N T T T S S B P A P S G C P P D S D A B AGCTCCAGCACAAGCGGAATCACAGGCGATAACACAACCACAAGCTCCGAGCCTGCCCCTAGCGGATGCCCTCCCGATAGCGATGCCGATA

RTQRRGRTGRGKPGIYRFVAPGBRPSGMFD

V R M Y V G G V B H R L E A A C N W T R G B R C D L E D R D GTGAGAATGTATGTGGGAGGCGTCGAGCATAGGCTCGAGGCTGCCTGTAACTGGACCAGAGGCGAAAGGTGTGACCTCGAGGATAGCGAT

BAQLHVWVPPLNVRGGRDAVILLMCVVHPT GAGGCTCAGCTCCACGTCTGGGTCCCCCCTCTGAATGTGAGAGGGGGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGTGCATCCCACA

HEDCIA #4 LGVRATRKTSERSQPRGRRQPIPKARPEG CTGGGAGTGAGAGCCACAAGGAAAACCTCCGAGAGAAGCCAACCCAGAGGCAGAAGGCAACCCATTCCCAAAGCCAGAAGGCCTGAGGGA

N V S V A H D G A G K R V Y Y L T R D P T T P L A R A A W B

S E P A P S G C P P D S D A E S Y S S M P P L E G E P G D P AGCGAACCCGCTCCCTCCGGCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCTCTGGAAGGCGGAACCCGGAGACCCT

I G G H Y V Q M A I I K L G A L T G T Y V Y N H L T P L R D ATCGGAGGCCATTACGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATCTGACACCCCTCAGGGAT

HepCla #126

PST B D L V N L L P A I L S P G A L V V G V V C A A I L R $\tt CCCTCCACCGAAGACCTCGTGAATCTCCCCCCCTATCCTCAGCCCTGGCGCTCTGGTGGTGGGAGTGGTCTGCGCTGCCATTCTGAGA$

HepCla #24

I L D M I A G A H W G V L A G I A Y P S M V G N W A K V L V

E G C G W A G W L L S P R G S R P S W G P T D P R R S R N GAGGGATGCGGATGGCTGGCTGGCTGCTCAGCCCTAGGGGAAGCAGACCCTCCTGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAAT

W T T Q G C N C S I Y P G H I T G H R M A W D M M M N N S P TGGACAACCCAAGGCTGTAACTGTAGCATTTACCCTGGCCATATCACAGGCCATAGGATGGCCTGGGACATGATGATGAACTGGAGCCCT

W V A M T P T V A T .R D G K L P A T Q L R R H I D L L V G S

HepCla #42

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R L W H Y P C T I N Y T I P K V R M Y V G G V B H R L B A A AGGCTCTGGCATTACCCTTGCACAATCAATTACACAATCTTTAAGGTCAGGATGTACGTCGGCGGAGTGGAACACAGACTGGAAGCCGGT

HepCla #172

V F C V Q P B K G G R K P A R L I V F P D L G V R V C B K M GTGTTTTGCGTCCAGCCTGAGAAAGGCGGAAAGGAAACCCGCTAGGCTCATCGTCTTCCCTGACCTCGGCGTCAGGGTCTGCGAAAAGATG

HepCla #10

MGYIPLVGAPLGGAARALAHGVRVLEDGVN ATGGGATACATTCCCCTCGTGGGAGCCCCTCTGGGAGGCGCTGCCAGGGCCCCTCGCCCATGGCGTCAGGGTCCTGGAAGACGGAGTGAAT

G G N A G R T T S G L V S L L T P G A K Q N I Q L I N T N G GGCGGAAACGCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCCCGGAGCCAAACAGAATATCCAACTGATTAACACAAACGGA

HepCla #13

LALLSCLTVPASAYQVRNSTGLYHVTNDCP CTGGCTCTGCTCAGCTGTCTGACAGTGCCTGCCTCTGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAAACGATTGCCCT

G R D K N Q V E G E V Q I V S T A A Q T F L A T C I N G V C GGCAGAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACAGCCGCTCAGACATTCCTCGCCACATGCATTAACGGAGTGTGT

HepCla #18
PATQLRRHIDLLVGSATLCSALYVGDLCGS

H^A P T G S G K S T K V P A A Y A A Q G Y K V L V L N P S V CACGCTCCCACAGGCTCCGGCAAAAGCACAAAGGTCCCCGCTGCCTATGCCGCTCAGGGATACAAAGTGCTCGTGCTCAACCCTAGCGTC

R T W A Q P G Y P W P L Y G N R G C G W A G W L L S P R G S AGGACATGGGCTCAGCCTGTCCCTGGCCCCTCTACGGAAACGAAGGCTGTGGCTGGGCCGGATGGCTCCTGTCCCCCAGAGGCTCC

T B D V V C C S M S Y S W T G A L V T P C A A E B Q K L P I ACCGAAGACGTCGTGTGTTGCTCCTACTCCTGGACAGGCGCTCTGGTCACCCCTTGCGCTGCCGAAGAGCCAAAAGCTCCCCATT

A L D T E V A A S C G G V V L V G L M A L T L S P Y Y K R Y GCCCTCGACACAGAGGTCGCCGCTAGCTGTCGCCGGAGTGGTCCTGGTCGGCCTCATGGCTCTGACACTGTCCCCCTATTACAAAAGGTAT

HepCla #38

W M N S T G F T K V C G A P P C V I G G A G N N T L H C P T

S V B B A C S L T P P H S A K S K P G Y G A K D V R C H A R AGCGTCGAGGAAGCCTGTAGCCTCACCCCTCCCCATAGCGCTAAGTCCAAGTTTGGCTATGGCGCTAAGGATGTGAGATGCCATGCCAGA

HepCla #119

I S G I Q Y L A G L S T L P G N P A I A S L M A P T A A V T ATCTCCGGCATTCAGTATCTGGCTGGCCTCAGCACACTGCCTGGCAATCCCGCTATCGCTTACGCTTCACAGCCGCTGTGACA

Q I V G G V Y L L P R R G P R L G V R A T R K T S E R S O P CAGATTGTGGGAGGCGTCTACCTCCTGCCTAGGAGAGGCCCTAGGCTCGGCGTCAGGGCTACCAGAAAGACAAGCGAAAGGTCCCAGCCT

HepCla #194

LHSYSPGEINRVAACLRKLGVPPLRAWRHR CTGCATAGCTATAGCCCTGGCGAAATCAATAGGGTCGCCGCTTGCCTCAGGAAACTGGGAGTGCCTCCCCTCAGGGCTTGGAGACACAGA

TARHTPVNSWLGNIIMPAPTLWARMILMTH ACCECTAGECATACCCCTGTGAATAGCTGGCTGGGAAACATTATCATGTTCGCTCCCACACTGTGGGCCAGAATGATTCTGATGACCCAT

ENL ETT M R S P V P T D N S S P P A V P Q S F Q V A H L GAGAATCTGGAAACCACAATGAGAAGCCCTGTGTTTTACCGATAACTCCAGCCCTCCCGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTC

HepCla #91

ATPPGSVTVPHPNIEEVALSTTGEIPFYGK

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GCCACACCCCTGGCTCCGTGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAA

HepCla #60

L V F D I T K L L A V F G P L W I L Q A S L L K V P Y F V CTGGTCTTCGATATCACAAAGCTCCTGCTCGCCGCTCTTCGGACCCCCTCTGGATCTCCGAAGCCTCCTGCTCAAGGTCCCCTATTTCGTC

HepCla #23

T A A L V M A Q L L R I P Q A I L D M I A G A H W G V L A G ACCECTECCTCGTGATGGCCCAACTGCTCAGGATTCCCCAAGCCATTCTGGATATGATTGCCGGAGCCCCATTGGGGAGTGCTCGCCGGA

HepCla #98

C N T C V T Q T V D F S L D P T F T I E T T T L P Q D A V S TGCAATACCTGTGTGACACAGACGAGAGGGGTTTCTCCCTGGATCCCACATCACAATCGAAACCACACCCTCCCCCAAGACGCTGTGTCC

HepCla #109

H G P T P L L Y R L G A V Q N E V T L T H P V T K Y I M T C CACGGACCCACACCCTCTGTATAGGCTCGGCGCTGTGCAAAACGAAGTGACACACCCTGTGACAAAGTATATCATGACCTGT

HepCla #179

A R V A I K S L T B R L Y V G G P L T N S R G B N C G Y R R GCCAGAGTGGCTATCAAAAGCCTCACCGAAAAGCCTCTCACCGAAAAGCCTCACCGAAAAGCCTCACCGAAAACTGTGGCTATAGGAGA

HenCla #39

C V I G G A G N N T L H C P T D C F R K H P E A T Y S R C G
TGCGTCATCGGAGGCGCTGGCAATAACACCTGCATTGCCCTACCGATTGCTTTAGGAAACACCCTGAGGCTACCTATAGCAGATGCGGA

HepCla #76

HepCla #138

N M W S G T F P I N A Y T T G P C T P L P A P N Y T F A L W AACATGTGGTCCGGCACATTCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCTCCCCGCTCCCAATTACACATTCGCTCTGTGG

HepCla #89

H S T D A T S I L G I G T V L D Q A E T A G A R L V V L A T CACTCCACCGATGCCACAAGCATTCTGGGAACCGGACCGGACCGGAGCCAGACTGGTGCTCGCCACA

HepCla #130

Y V P E S D A A A R V T A I L S S L T V T Q L L R R L H Q W TACTICCCCGAAAGCGATGCCGCCCAACTGCCCCAACTGCCCCAACTGCCCCAACTGCCCCAACTGCATCAGTGG

HepCla #8

R P S W G P T D P R R R S R N L G K V I D T L T C G F A D L AGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACACACTGACATGCGGATTCGCTGACCTC

HepCla #33

HepCla #115

BECSQHLPYIBQGMMLAEQFKQKALGLLQTGAGGAATGCTCCCAGCATCTGCCTTACATTGAGCAAGGCATGATGCTCCCCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACA

HepCla #107

Y Q A T V C A R A Q A P P P S W D Q M W K C L I R L K P T L TACCAAGCCACAGTGTGTGCCAGGCCCAAGCCCCTCCCCCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTC

HepCla #34

HepCla #131

HepCla #161

D L S D G S W S T V S S E A G T E D V V C C S M S Y S W T G GACCTCAGCGATGGCTCCTCGACCTCAGCCTCAGCCTCAGCTCGCACAGAGGATGTGGTCTGTAGCATGAGCTATAGCTGGACCGGA

HepCla #108

W D Q M W K C L I R L K P T L H G P T P L L Y R L G A V Q N
TGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGCCCTACCCCTCTGCTCTACAGACTGGGAGCCGTCCAGAAT

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HepCla #116

L A E Q F K Q K A L G L L Q T A S R Q A B V I A P A V Q T N CTGGCTGAGCAATCAACAGAAGCCCTCGGCCTCCTGCAAACCGCTAGCAGACAGGCTGAGGTCATCGCTCCCGCTGTGCAAACCAAT

HepCla #118

W Q K L E V F W A K H M W N F I S G I Q Y L A G L S T L P G TGGCAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTTCATTAGCGGAATCCAATACCTCGCCGGACTGTCCACCCTCCCCGGA

HepCla #129

LIAFASRGNHVSPTHYVPESDAAARVTAIL

HenCla #10

A T L C S A L Y V G D L C G S V F L V G Q L F T F S P R R H GCCACACTGTGTAGGGCTCTTGTATGTGGGAGACCTCTGCGGAAGGCTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGCAT

HepCla #102

S S V L C E C Y D A G C A W Y E L T P A E T T V R L R A Y M AGCTCCGTGCTCTCGCGAATGCTATGACGCTGGCTGCTGCTACGACTGACACCCGCTGAGACAACCGTCAGGCTCAGGCTTACATG

HepCla #122

HepCla #29

S W H I N S T A L N C N B S L N T G W L A G L F Y Q H K F N AGCTGGCACATTAACTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACAAATTCAAT

HepCla #164

HepCla #1

A A M S T N P K P Q R K T K R N T N R R P Q D V K F P G G G GCCCCTATGTCCACCAATCCCAAAACCCAAAACCAAAAACCAAAAAGGAATACCAATAGGAGACCCCAAGACCTCAAGTTTCCCCGAGGCGGA

HepCla #106

SQTKQSGENPPYLVAYQATVCARAQAPPPS
AGCCAAACCAAACAGTCCGGCGAAACTTTCCCTACTGGCCTATCAGGCTCACGTCTGCGCTAGGGCTCAGGCTCCCCTCCC

HepCla #36

A PTYSWGANDTDVFVLNNTRPPLGNWFGCTGCCCCTCTGGGAAACTGGTTCGGATGCACA

HepCla #156

V P P P R K K R T V V L T E S T L S T A L A E L A T K S F G GTGCCTCCCCCTAGGAAAAAGAGAACCGTCGTCCTCCCCCAAAGCACACTGTCCACCGCTCTGCCTCGAGACCCCCACAAAGTCCTTCGGA

HepCla #165

S T T S R S A C Q R Q K K V T P D R L Q V L D S H Y Q D V L AGCACAACCTCCAGGTCCGCCTCTAGAGACAAAAGGTCACCTTTGACAGACTGCAAGTGCTCGACTCCACTATCAGGATGTGCTC

HepCla #90

D Q A E T A G A R L V V L A T A T P P G S V T V P H P N I E GACCAAGCCGAAACCGCTGGCGCTGGCTCCCTGCCTACCGCTACCCCTTCCCGGAAGCGTCACCGCTCCCCATCCCAATATCGAA

HepCla #141

FHYVTGMTTDNLKCPCQVPSPEFFTELDGV TTCCATTACGTCACCGGAATGACAACCGATAACCTCAAGTGTCCCTGCAGGTCCCCCCCGAATTCTTTACCGAACTGGATGGCTC

HepCla #198

HepCla #117

A S R Q A E V I A P A V Q T N W Q K L E V P W A K H N W N F GCCTCCAGGCAAGCGAAGTGATTGCCCCTCCCGCCCTCCAGACAAACTGGCAGAGTGTTTTTGGGCTAAGCATATGTGGAACTTT

HepCla #181

CRASGVLTTSCGNTLTCYIKARAACRACGCGCTGCGGAAACACACTGACATGCTATATCAAAGCCAGAGCCGCTTGCAGAGCCGCTTGCGCTCTC

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HepCla #166

HepCla #180

G P L T N S R G B N C G Y R R C R A S G V L T T S C G N T L GGCCCTCTGACAAACTCCACAAGCTGTGGCAATACCCTC

HepCla #136

I M H T R C H C G A E I T G H V K N G T M R I V G P R T C R ATCATGCACACAGGTGTCACTGTGGCGCTGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGA

HepCla #144

EVSPRVGLHEYPVGSQLPCEPPDVAVLTS
GAGGTCAGCTTTAGGGTCGGCCTCCACGAATACCCTGTGGGAAGCCAACTGCCTTGCGAACCCGAACCCGATGTGGCTGTCCTCACCTCC

HepCla #167

KEVKAAASKVKANLLSVEEACSLTPPHSAK AAGGAAGTGAAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCGTGCGAAGAGGGCTTGCTCCCTGACACCCCCCTCACTCCGCCAAA

HepCla #59

G R D A V I L L M C V V H P T L V F D I T K L L A V F G P GGCAGAGACGCTGTGTTGTGTCTCTGGTCCTCCTGGTGTTTTGACCATACCTAAACTGCTCCTGGCTGTTTTGGCCCT

HepCla #146

HepCla #78

S P R P I S Y L K G S S G G P L L C P A G H A V G I F R A A AGCCCTAGGCCTATCTCCTACGCAAGGGAAGCTCCGGCGGACCCCTCCTGTGTCCCGCTGGCCATGCCGTCGGCATTTTCAGAGCCGCT

HepCla #32

D P D Q G W G P I S Y A N G S G P D Q R P Y C W H Y P P K P GACTITGACCAAGGCTGGGGCCCTATCTCCTAGGCTAAGGCTAAGGCTATCGCCTATCCCCCTAAGCCT

HepCla #128

HepCla #50

C L W M M L L I S Q A B A A L B N L V I L N A A S L A G T H
TGCCTCTGGATGATGCTCCTGATTAGCCAAGCCGGAGCCCGTTGGAAAACCTCGTGATTCTGAATGCCGCTAGCCTCGCGGAACCCCAT

HepCla #114

I I P D R E V L Y R E P D E M E E C S Q H L P Y I E Q G M M ATCATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAGAGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATG

HepCla #47

L I H L H Q N I V D V Q Y L Y G V G S S I A S W A I K W E Y CTGATTCACCTCCACCAAAACATTGTGGATGTGCAATACCTCTACGGATGTGGAAGCTCCATCGCTAGCTGGGCCCATTAAGTGGGAGTAT

HepCla #200

HepCla #85

A A T L G F G A Y M S K A H G I D P N I R T G V R T I T T G GCCCTACCCTCGCCTTTGGCCCTTACATCAGCAAAGCCCCATGGCATTGACCCTAACATTAGGACAGCCGTCAGGACAATCACAACCGGA

HenCla #6:

R V Q G L L R I C A L A R K M I G G H Y V Q M A I I K L G A AGGGTCCAGGGACTGCTCAGGATTTGCGCTCTGGCTAGGAAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCCGCGCCT

HepCla #153

R P A Q A L P V W A R P D Y N P P L V B T W K K P D Y B P AGGAGATTCGCTCAGGCTCTGGCCTGTGGGCCCAGACCCGATTACAATCCCCCTCTGGTCGAGACATGGAAAAAGCCTGACTATGAGCCT

HepCla #72

TAAQTPLATCINGVCWTVYHGAGTRTIASPACCGCTGCCCAAACCTTCTGGCTACCATGGCCCTACCATGGCGCTCGCACAAGGACAATCGCTAGCCCT

HepCla #65

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W A H N G L R D L A V A V E P V V P S Q M E T K L I T W G A TGGGCTCACAATGGCTCAGGGAACCCAGGGAACCGGCGGTTTTAGCCAAATGGAACCAAACTGATTACCTGGGGCGCT

HepCla #74

HepCla #151

HepCla #64

LTGTYVYNHLTPLRDWAHNGLRDLAVAVEP CTGACAGGCACATACGTCTACAATCACCTCTCAGGAGACTGGGGCCCATAACGGACTGAGAGACTCGCCGTCGCCGTCGAGGCCT

HepCla #80

V C T R G V A K A V D F I P V B N L B T T M R S P V F T D N GTGTGTACCAGAGGGGTCGCCAAAGCCGTCGACTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAAT

HepCla #95

HepCla #111

HepCla #97

A L M T G Y T G D F D S V I D C N T C V T Q T V D F S L D P GCCCTCATGACGGCTATACCGGGGGACTTTGACTCCGTGATTGACTCTAACACGTCGACCCCAAACCGTCGACTTTAGCCTCGACCCT

HepCla #2

N T N R R P Q D V K F P G G G Q I V G G V Y L L P R R G P R AACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTGGCGGAGGCCAAATCGTCGGCGGAGTGTATCTGCTCCCCAGAAGGGGACCCAGA

HepCla #11

R A L A H G V R V L B D G V N Y A T G N L P G C S F S I F L AGGGCTCTGGCTCACGGAGTGAGGATGCTCGAGGATGTGCCTCACCTAGCATTTTCCTC

HepCla #169

S K F G Y G A K D V R C H A R K A V A H I N S V W K D L L R AGCAAATTCGGATACGGAGCCAAAGACCTCAGGTCTCACGCTAGGAAAGCCCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAA

HepCla #28

TPGAKQNIQLINTNGSWHINSTALNCNESL ACCCCTGGGGCTAAGCAAACATTCAGCTCAATACCAATGGCTCCTGGCATATCAATAGCACAGCCCTCAACTGTAACGAAAGCCTC

HepCla #30

N T G W L A G L P Y Q H K P N S S G C P E R L A S C R R L T AACACAGGCTGGCTGGCTGTCTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCCTGAGAGACTGGCTAGCTGAGGAGACTGACA

HepCla #49

V V L L F L L L A D A R V C S C L W M M L L I S Q A E A A L GTGGTCCTGCTCTCCTCCTGCTGGATGCCAGGCTGAGGCTGCCCTC

HepCla #192

D C E I Y G A C Y S I E P L D L P P I I Q R L H G L S A F S GACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCTATCATCAGAGACTGCATGGCCTCAGCGCTTTCTCC

HepCla #73

W T V Y H G A G T R T I A S P K G P V I Q M Y T N V D Q D L TGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTACACAAACGTCGACCAAGACCTC

HepCla #101

Y R F V A P G B R P S G M F D S S V L C B C Y D A G C A W Y TACAGATTCGTCGCCCCTGGCGAAAGGCCTAGCGGAATGTTTGACTCCAGCGTCCTGTCTGAGTGTTTACGATGCCGGATGCCTTGGTAT

HepCla #45

R S E L S P L L L S T T Q W Q V L P C S F T T L P A L S T G
AGGTCCGAGCTCAGCCCTCTGCTCCACCACACAGTGGCAGGTCCTGCTCTTCACAACCCTCCCCGGTCTGTCCACCGGA

HepCla #195

LRKLGVPPLRAWRHRARSVRARLLARGGRA

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CTGAGAAAGCTCGGCGTCCCCCCTCTGAGAGCCTGGAGGGCATAGGGCTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGGCGGAAGGGCT

HepCla #121

S P L T T S Q T L L P N I L G G W V A A Q L A A P G A A T A AGCCCTCTGACAACCTCCCAGACACTGCTCTCAATATCCTCGGGGGATGGGTCGCCGCTCAGCTCGCCGCTCCCGGAGCCGCTACCGCT

HepCla #61

L W I L Q A S L L K V P Y F V R V Q G L L R I C A L A R K M CTGTGGATCCTCCAGGCTAGCCTCCTGAAAGTGCCTTACTTTGTGAGAGTGCAGAGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATG

HepCla #137

V K N G T M R I V G P R T C R N M W S G T F P I N A Y T T G GTGAAAAACGGAACCTTGGGGACCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGGA

HepCla #92

EVALSTTGBIPFYGKAIPLBVIKGGRHLIPGAGGTCGCCCTCAGCACACCAGAGAGAGACTCCTCTTTACGGAAAGGCTATCCCTCTCGAAGTGATTAAGGGAGGCAGACACCTCATCTTT

HepCla #188

HepCla #140

R V S A E E Y V E I R R V G D F H Y V T G M T T D N L K C P AGGGTCAGCGCTGAGGAATACGTCGAGAGTTAGGAGGAGTTCACTATGTGACAGGCATGACCACAGACAATCTGAAATGCCCT

HepCla #155

PVVHGCPLPPPRSPPVPPRKKRTVVLTES

HepCla #157

T L S T A L A E L A T K S F G S S S T S G I T G D N T T T S ACCCTCAGCACAGCCCTCGCCGAACTGCCTACCAAAAGCTTTGGCTCCAGCTCCACCTCCGCCATTACCGGAGACAATACCACAACCTCC

HepCla #135

V S C Q R G Y K G V W R G D G I M H T R C H C G A E I T G H
GTGTCCTGCCAAAGGGGATACAAAGGCGTCTGGAGAGGCGATGCCATTATGCATACCAGATGCCATTGCGAAGCCGAAATCACAGGCCAT

HepCla #20

V P L V G Q L P T F S P R R H W T T Q G C N C S I Y P G H I GTGTTTCTGGTCGGCCAACTGTTTACCCTTTAGCCCTAGGAGACACTGGACCACACAGGGATGCAATTGCTCCATCTATCCCGGACACATT

HepCla #123

FVGAGLAGAAIGSVGLGKVLVDILAGYGAG TTCGTCGGCGCTCGCCGGAGCCCCTTTCGGAAGCGTCGCCTCGCAAAGTCCTCGTGGATATCCTCGCCGGATACGGAGCCCGGA

HepCla #133

D I W D W I C B V L S D F K T W L K A K L M P Q L P G I P F GACATTTGGGATTGGGATTGCGGATTCCCTTTTCAAAACCTGGCTGAAAGCCCAAACTGATGCCCCAACTGCCATTCCCTTT

HepCla #15

N S S I V Y B A A D A I L H T P G C V P C V R B G N A S R C AACTCCAGCATTGTGTGTGTGTGTGTGTGTGTGTGGGTAGGGAAGGCAATGCCTCCAGGTGT

HepCla #31

S S G C P B R L A S C R R L T D F D Q G W G P I S Y A N G S AGCTCCGGCTGCCGAAAGGCTCCTGCAGAAGGCTCACCGATTCGATCAGGGATGGGGACCCATTAGCTATGCCAATGGCTCC

HepCla #178

HenCla #69

V S K G W R L L A P I T A Y A Q Q T R G L L G C I I T S L T GTGTCCAAGGGATGGAGGACTGCTCGCCCTATCACAGCCTATGCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCCTGACA

HepCla #191

FFSVLIARDQLEQALDCEIYGACYSIEPLD

HepCla #142

C Q V P S P B P F T B L D G V R L H R P A P P C K P L L R B TGCCAAGTGCTTAGCCCTGCGGATTTTTCACAGAGCTCGACGGAGACTGCATAGGTTTGCCCCTCCTGTAAGCCCTCTCAGGGAA

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HepCla #182

T C Y I K A R A A C R A A G L Q D C T M L V C G D D L V V I
ACCTGTTACATTAAGGCTAGGGCTGCTAGGGCTGCCAGACTGCAGACTGTACCATGCTGGTCTGGGAGACGATCTGGTCGTGATT

HepCla #86

I D P N I R T G V R T I T T G S P I T Y S T Y G K P L A D G ATCGATCCCAATATCAGAACCGGAAGTTTCTGGCTGACGGA

HepCla #44

C N W T R G B R C D L B D R D R S E L S P L L L S T T Q W Q TGCAATTGGCAAGGGGAGGGGAGACGGAGACGGAACTGTCCCCCCTCCTGCTCAGCACAACCCAATGGCAA

HepCla #22

T G H R M A W D M M M N W S P T A A L V M A Q L L R I P Q A ACCEGACACAGAATEGCTTEGGATATGATGATTGATTCCTCAGGCTCTCAGCCTCTTGGTCATCGCTCAGCTCTTGAGAATCCCTCAGGCT

HepCla #127

PGALVVGVCAAILRRHVGPGEGAVQWMNRCCCCGGAGCCCTCGCGAAGGCGCTCTCCAATGGATGACAGA

HepCla #149

HepCla #105

B G V F T G L T H I D A H F L S Q T K Q S G E N F P Y L V A GAGGGAGTGTTTACCGGACTGACACACACTTGACGCTCACTTCTCTCCCAGACAAAGCGAAAGCGAAGAGAATTTCCCTTACCTCGTGGCT

HepCla #9

RGRRQPIPKARRPEGRTWAQPGYPWPLYGN AGGGGAAGGACAGCCTATCCCTAAGGCTAGGAGACCCGAAGCCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAAT

HepCla #173

L I V F P D L G V R V C E K M A L Y D V V S K L P L A V M G
CTGATTGTGTTTCCCGATCTGGGAGTGAGAGAGTGTGTGAGAAAATGGCTCTGTTGAGGTGCTCCCAAGCTCCCCCTCGCCGTCATGGGA

HepCla #12

HepCla #124

L G K V L V D I L A G Y G A G V A G A L V A F K I M S G E V CTGGGAAAGGTCCTGGTCGACATTCTGGCTGGCTATGCCGTGGCGTCGCCGGAGCCCTCGTGGCTTTCAAAATCATGAGGGGAGAGGTC

HepCla #160

HepCla #150

RQEMGGNITRVESENKVVILDSFDPLVAEE
AGGCAAGAGATGGCGAAAACAAAGTGGTCATCCTCGACTCCTTCGATCCCTCGTGGCTGAGGAA

HepCla #75

HepCla #88

G C S G G A Y D I I I C D E C H S T D A T S I L G I G T V L GGCTGTAGCGGAGGCGCTTACGATATCATTATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCCGCATTGGCACAGTGCTC

HepCla #99

T F T I E T T T L P Q D A V S R T Q R R G R T G R G K P G I ACCTITACCATTGAGACCACACTGCCTCAGGATGCCGTCAGCAGAACCCCAAAGGAGAGCAGAACCCGAAAGCAGAACCACACTGCCTCAGGATGCCGTCAGCAGAACCCCAAAGGAGAGGAGACCCGAAACCACACTGCCTCAGCATGCCATT

HepCla #40

D C F R K H P B A T Y S R C G S G P W I T P R C L V D Y P Y GACTGTTTCAGAAAGCATCCCGAACCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTCGACTATCCCTAT

HepCla #201

LAAGVGIYLLPNRAA

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HepCla #163

A L V T P C A A E E Q K L P I N A L S N S L L R H H N L V Y
GCCCTCGTGACACCCTGTGCCGCTGAGGAACAGAAACTGCCTATCAATGCCCTCAGGAATAGCCTCCTGAGACACCATAACCTCGTGTAT

HepCla #132

I S S E C T T P C S G S W L R D I W D W I C B V L S D F K T ATCTCCAGCGAATGCACCACTTGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGTAGGGTCCTGTCCGACTTTAAGACA

HepCla #134

W L K A K L M P Q L P G I P P V S C Q R G Y K G V W R G D G
TGGCTCAAGGCTAAGGCTCATGCCTCAGGTCCCCGGAATCCCTTTCGTCAGCTGTCAGGAGGGGAGTTTTGGAGGGGAGTGTGAGGGGAGACGGA

HepCla #41

S G P W I T P R C L V D Y P Y R L W H Y P C T I N Y T I F K
AGCEGACCCTEGATCACACCCAGATGCCTCGGATTACCCTTACCAGACTGTGGCACTATCCCTGTACCATTAACTATACCATTTTCAAA

Artificial Protein:

VIPVRRRGDSRGSLLSPRPISYLKGSSGGPARRGREILLGPADGMVSKGWRLLAPITAYARLHRFAPPCKPLLREEVSPRVGLHEYPVGSVVPSQMET KLITWGADTAACGDIINGLPVSLLCPAGHAVGIFRAAVCTRGVAKAVDFIPVCVVIVGRIVLSGKPAIIPDREVLYREFDEMPCTPLPAPNYTFALWR vsabbyvbirrvgdalydvvsklplavmgssygfqyspgqrvbfiswclwwlqyfltrvbaqlhvwvpplavrgenlvilnaaslagthglvsflvff CFAWYLLPPIIQRLHGLSAFSLHSYSPGBINRVAACNPPLVBTWKKPDYEPPVVHGCPLPPPRSPPGVGSSIASWAIKWBYVVLLPLLLADARVCSLN ntrpplgnwfgctwmnstgftkvcgappfteamtrysappgdppqpeydlellitscsswpllllllalpqrayaldtevaascggvvlqotrgllgci ITSLTGRDKNQVEGEVQIVSSSPPAVPQSPQVAHLHAPTGSGKSTKVPAANTPGLPVCQDHLEFWEGVFTGLTHIDAHFLVLLLFAGVDAETHVTGGN agritsglvsllevtlthpvtkyimtcmsadlevvtstwvlvvglmaltlspyykryiswclwwlqyfltrvaicgkylfnwavrtklkltpiaaagr ldls1ayfsmvGnwakvlvvlllfagvdaethvtrlargsppsmasssasqlsapslkatctanglvsplvffcfawylkgrwvpgavyalygmqlpc epepdvavltsmltdpshltabaagrdsvtpidttimaknevfcvqpekggrkparyaaqgykvlvlnpsvaatlgfgaymskahgvrnstglyhvtn DCPNSSIVYEAADAILHTSSYGFQYSPGQRVEFLVQAWKSKKTPMGFSDTAACGDIINGLPVSARRGREILLGPADGMSQLSAPSLKATCTANHDSPD ablieanllwnpaiaslmaftaavtsplitsqtllfniiglvqawkskktpmgfsydtrcfdstvtesdiderbisvpabilrksrrfaqalpvwarp DYMPAPTLNARMILMTHFFSVLIARDQLEQALSVIPTSGDVVVVATDALMTGYTGDFDSVIDCHSKKKCDBLAAKLVALGINAVAYYRGLDVVLPCSF ttlpalstglihlhqnivdvqylykgrwvpgavyalygmwpllllllalpqrayspitystygkpladggcsggaydiiicdbcarsvrarllarggr AAICGKYLFNWAVRTKKAVAHINSVWKDLLEDSVTPIDTTIMAKNEFTPSPVVVGTTDRSGAPTYSWGANDTDVFVPGCVPCVREGNASRCWVAMTPT VATROGKLQDCTMLVCGDDLVVICESAGVQEDAASLRAVAGALVAFKIMSGEVPSTEDLVNLLPAILSYDTRCFDSTVTESDIRTBRAIYQCCDLDPQ eltpabttvrlraymntpglpvcqdhlefwpqpbydlblitscssnvsvahdgagkrvyylgkvidtltcgfadlmgyiplvgaplggaaaiplevik GGRHLIFCHSKKKCDELAAKLVGGVLAALAAYCLSTGCVVIVGRIVLSGKPACESAGVQEDAASLRAFTEAMTRYSAPPGDPGWFTAGYSGGDIYHSV SHARPRWFWFCLLLSSSTSGITGDWTTTSSEPAPSGCPPDSDAERTQRRGRTGRGKPGIYRFVAPGERPSGMFDVRMYVGGVEHRLEAACNWTRGERC ${\tt DLEDRDEAQLHVWVPPLNVRGGRDAVILLMCVVHPTLGVRATRKTSERSQPRGRRQPIPKARRPEGNVSVAHDGAGKRVYYLTRDPTTPLARAAWESE$ PAPSGCPPDSDAESYSSMPPLEGEPGDPIGGHYVQMAIIKLGALTGTYVYNHLTPLRDPSTEDLVNLLPAILSPGALVVGVVCAAILRILDMIAGAHW GVLAGIAYFSMVGNNAKVLVEGCGWAGWLLSPRGSRPSWGPTDPRRRSRNWTTQGCNCSIYPGHITGHRMAWDMMNWSPWVAMTPTVATRDGKLPAT QLRRHIDLLVGSRLWHYPCTINYTIFKVRMYVGGVEHRLEAAVFCVQPEKGGRKPARLIVFPDLGVRVCEKMMGYIPLVGAPLGGAARALAHGVRVLE DGVNGGNAGRTTSGLVSLLTPGAKQNIQLINTNGLALLSCLTVPASAYQVRNSTGLYHVTNDCPGRDKNQVEGEVQIVSTAAQTFLATCINGVCPATQ LRRHIDLLVGSATLCSALYVGDLCGSHAPTGSGKSTKVPAAYAAQGYKVLVLNPSVRTWAQPGYPWPLYGNEGCGWAGWLLSPRGSTEDVVCCSMSYS WTGALVTPCAABBQKLPIALDTEVAASCGGVVLVGLMALTLSPYYKRYWMNSTGFTKVCGAPPCVIGGAGNNTLHCPTSVBBACSLTPPHSAKSKFGY gakdvrcharisg-qylaglstlpgnpaiaslmaptaavtqivggvyllprrgprlgvratrktsersqplhsyspgbinrvaaclrklgvpplrawr HRTARHTPVNSWLGNI IMPAPTLWARMILMTHENLETTMRSPVFTDNSSPPAVPQSFQVAHLATPPGSVTVPHPNIEBVALSTTGBI PFYGKLVFDIT klllavfgplwilqasllkvpyfvtaalvmaqllripqaildmiagahwgvlagcntcvtqtvdfsldptftietttlpqdavshgptpllyrlgavq nbvtlthpvtkyimtcarvaiksltbrlyvggplinsrgencgyrrcviggagnntlhcptdcfrkhpbatysrcgicgssdlylvtrhadvipvrrr gdsrgsllnnwsgtffinayttgpctplpapnytfalwhstdatsilgigtvldqaetagarlvvlatyvpesdaaarvtailssltvtqllrrlhqw RPSWGPTDPRRRSRNLGKVIDTLTCGFADLGPDQRPYCWHYPPKPCGIVPAKSVCGPVYCEECSQHLPYIEQGMMLAEQFKQKALGLLQTYQATVCAR aqapppswdqmwkclirlkptlcgivpaksvcgpvycptpspvvvgttdrsgssltvtqllrrlhowissbcttpcsgswlrdlsdgswstvssbagt edvvccsmsyswtgmdqmwkclirlkptlhgptpllyrlgavqnlaeqfkqkalgllqtasrqaeviapavqtnwqklevfwakhmwnfisgiqylag LSTLPGLIAFASRGNHVSPTHYVPBSDAAARVTAILATLCSALYVGDLCGSVPLVGQLFTFSPRRHSSVLCECYDAGCAWYBLTPAETTVRLRAYMGW VAAQLAAPGAATAPVGAGLAGAAIGSVGSWHINSTALNCNESLNTGWLAGLPYQHKPNNALSNSLLRHHNLVYSTTSRSACQRQKKVTAAMSTNPKPQ rktkritnrrpodvkppgggsqtkqsgenppylvayqatvcaraqapppsaptyswgandtdvfvlnntrpplgnwfgctvppprkkrtvvltestls TALABLATKSPGSTTSRSACQRQKKVTFDRLQVLDSHYQDVLDQAETAGARLVVLATATPPGSVTVPHPNIEFHYVTGMTTDNLKCPCQVPSPEFFTB ldgvlkltpiaaagrldlsgwftagysggdiyhsasrqaeviapavqtnwqklbvfwakhmwnfcrasgvlttscgntltcyikaraacraaglfdrl QVLDSHYQDVLKEVKAAASKVKANLLGPLTNSRGENCGYRRCRASGVLTTSCGNTL1MHTRCHCGAB1TGHVKNGTMR1VGPRTCREVSFRVGLHEYP vgsqlpcbpbpdvavltskbvkaaaskvkanllsvbbacsltpphsakgrdavillmcvvhptlvfditklllavpgpmltdpshitabaagrrlarg SPPSMASSSASPRPISYLKGSSGGPLLCPAGHAVGIFRAADFDQGWGPISYANGSGPDQRPYCWHYPPKPRHVGPGEGAVQMMNRLIAFASRGNHVSP THCLWMMLLISQABAALBNLVILNAASLAGTHIIPDRBVLYRBFDEMBECSQHLPYIBQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARP rwfwpcllllaagvgiyllpnraaaatlgpgaymskahgidpnirtgvrtittgrvqgllricalarkmigghyvqmaiiklgarrfaqalpvwarpd YNPPLVETWKKPDYEPTAAQTFLATCINGVCWTVYHGAGTRTIASPWAHNGLRDLAVAVEPVVFSQMETKLITWGAKGPVIQMYTNVDQDLVGWPAPQ GSRSLTPCKVVILDSFDPLVAEEDERBISVPAEILRKSLTGTYVYNHLTPLRDWAHNGLRDLAVAVEPVCTRGVAKAVDPIPVENLETTMRSPVFTDN alginavayyrgldvsviptsgdvvvvatdmsadlbvvtstmvlvggvlaalaayclstgalmtgytgdfdsvidcntcvtqtvdpsldpntnrrpqd vkfpgggqivggvyllprrgprralahgvrvledgvnyatgnlpgcspsiplskfgygakdvrcharkavahinsvmkdlletpgakqniqlintngs WHINSTALNCNESLNTGWLAGLPYQHKFNSSGCPERLASCRRLTVVLLPLLLADARVCSCLWMHLLISQABAALDCEIYGACYSIBPLDLPPIIQRLH GLSAFSWTVYHGAGTRTIASPKGPVIQMYTNVDQDLYRFVAPGERPSGMFDSSVLCECYDAGCAWYRSELSPLLLSTTQWQVLPCSFTTLPALSTGLR Klgvpplrawrhrarsvrarllarggrasplttsqtllfnilggwvaaqlaapgaatalnilqasllkvpypvrvqgllricalarkmvkngtmrivg prtcrnmwsgtppinayttgevalsttgeippygkaiplevikggrhlipltrdpttplaraawbtarhtpvnswlgniirvsaebyvbirrvgdphy VTG#TTDNLKCPPVVHGCPLPPPRSPPVPPPRKKRTVVLTESTLSTALABLATKSFGSSSTSGITGDNTTTSVSCQRGYKGVWRGDGIMHTRCHCGAE itghvflvgqlftfsprrhwttqgcncsiypghifvgaglagaaigsvglgkvlvdilagygagdiwdwicevlsdfktwlkaklmpqlpgipfnssi vyeaadailhtpgcvpcvregnasrcssgcperlascrrltdpdgwgpisyangsrteeaiyoccdldpoarvaikslterlyvgvskgwrllapit ayaqqtrgllgciitsltpfsvliardqleqaldceiygacysibpldcqvpspeppteldgvrlhrfappckpllrbtcyikaraacraaglqdctm

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LVCGDDLVVIIDPNIRTGVRTITTGSPITYSTYGKFLADGCNWTRGERCDLEDRDRSELSPLLLSTTQWQTGHRMAWDMMNWSPTAALVMAQLLRIP QAPGALVVGVVCAAILRRHVGPGEGAVQMMNRHDSPDABLIEANLLWRQEMGGNITRVESENEGVFTGLTHIDAHFLSQTKQSGENFPYLVARGRRQP IPKARRPEGRTWAQPGYPWPLYGNLIVPPDLGVRVCEKMALYDVVSKLPLAVMGYATGNLPGCSPSIFLLALLSCLTVPASAYQLGKVLVDILAGYGA GVAGALVAFKIMSGEVSYSSMPPLEGEPGDPDLSDGSWSTVSSEAGRQEMGGNITRVESENKVVILDSFDPLVAEEVGWPAPQGSRSLTPCTCGSSDL YLVTRHADGCSGGAYDIIICDECHSTDATSILGIGTVLTFTIETTTLPQDAVSRTQRRGRTGRGKPGIDCFRKHPEATYSRCGSGEWITPRCLVDYPY LAAGYGIYLLPMRAAALVTPCAAEEQKLPINALSNSLLRHNLVYISSECTTPCSGSWLRDIWDWICEVLSDFKTWLKAKLMPQLPGIPFVSCQRGYK GVWRGDGSGPWITPRCLVDYPYRLMHYPCTINYTIFK

Artificial DNA:

 $\tt GTGATTCCCGTCAGGAGGGGGAGGCTCCAGGGGGAAGCCTCCTGTCCCCCAGACCCCATTAGCTATCTGAAAGGCTCCAGCGGAGGCCCTGCCAGAAG$ GGGAAGGGAAATCCTCCTGGGACCCGCTGACGGAATGGTCAGCAAAGGCTGGAGGCTCCTGGCTCCCATTACCGCTTACGCTACGCTCCACAGATTCG CTCCCCCTTGCAAACCCCTCCTGAGAGAGGGAAGTGTCCTTCAGAGTGGGACTGCATGAGTATCCCGTCGGCTCCGTGGTCTTCTCCCAGATGGAGACA CTTTAGGGCTGCCGTCTGCACAAGGGGAGTGGCTAAGGCTGTGGATTTCATTCCCGTCTGGTCGTGATTGTGGGAAGGATTGTGCTCAGCGGAAAGC GTGTCCGCCGAAGAGTATGTGGAAATCAGAAGGGTCGGCGATGCCCTCTACGATGTGGTCAGCAAACTGCCTCTGGCTGTGATGGGCTCCAGCTATGG CITTCAGTATAGCCCTGGCCAAAGGGTCGAGTTTATCTCCTGGTGTCTGTGGTGGTCCAGTATTTCCTCACCAGAGTGGAAGCCCAACTGCATGTGT TGCTTTGCCTGGTACCTCCTGCCTCCCATTATCCAAAGGCTCCACGGACTGTCCGCCTTTAGCCTCCACTCCTACTCCCCCGGAGAGATTAACAGAGT GGCTGCCTGTAACCCTCCCCCCGGAAACCTGGAAGAAACCCGATTACGAACCCCCTGTGGTCCACGGATGCCCTCTGCCTCCCCCTAGGTCCCCCC CTGGCGTCGGCTCCAGCATTGCCTCCTGGGCTATCAAATGGGAATACGTCGTGCTCCTGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCCCTGAAT AACACAAGGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCTTTCACAGAGGCTAT GACAAGGTATAGCGCTCCCCTGGCGATCCCCCTCAGCCTGAGTATGACCTCGAGCTCATCACAAGCTGTAGCTCCTGGCCCTCTGCTCCTGCTCCTGC TCGCCCTCCCCAAAGGGCTTACGCTCTGGATACCGAAGTGGCTGCCTCCTGCGGAGGCGTCGTGCTCCAGCAAACCAGAGGCCTCCTGGGATGCATT ATCACAAGCCTCACCGGAAGGGATAAGAATCAGGTCGAGGGGAGAGGTCCAGATTGTGTCCAGGTCCCCCCTGCCGTCCCCCAAAGCTTTCAGGTCGC GGTCGTGACAAGCACATGGGTCCTGGTCGTGGGACTGATGGCCCTCACCCTCAGCCCTTACTATAAGAGATACATTAGCTGGTGGCTCTGGTGGCTGC AATACTTTCTGACAAGGGTCGCCATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCAGA CTGGATCTGTCCATCGCTTACTTTAGCATGGTGGGAAACTGGGCCAAAGTGCTCGTGGTCCTGCTCCTGTTTGCCGGAGTGGATGCCGAAACCCATGT TOGTGTCCTTCCTCGTGTTTTTCTGTTTCGCTTGGTATCTGAAAGGCAGATGGGTCCCCCGGAGCCGTCTACGCTCTGTATGGCATGCAGCTCCCCTGT GAGCCTGAGCCTGACGTCGCCGTCCTGACAAGCATGCTGACAGACCCTAGCCATATCACAGCCGAAGCCGCTGGCAGAGACTCCGTGACACCCATTGA CACAACCATTATGGCTAAGAATGAGGTCTTCTGTGTGCAACCCGAAAAGGGGAGGCAGAAAGCCTGCCAGATACGCTGCCCAAGGCTATAAGGTCCTGG TCCTGAATCCCTCCGTGGCTGCCACACTGGGGATTCGGAGCCTATATGTCCAAGGCTCACGGAGTGAGAAACTCCACCGGACTGTATCACCGACT GACTGTCCCAATAGCTCCATCGTCTACGAAGCCGCTGACGCTATCCTCCACACAAGCTCCTACGGATTCCAATACTCCCCGGACAGAGAGTGGAATT CCTCGTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGGATTCTCCGACACAGCCGCTTGCGGAGACATTATCAATGGCCTCCCCGTCAGCGCTAGGA GAGGCAGAGAGATTCTGCTCGGCCCTGCCGATGGCCATGAGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTACCGCTAACCATGACTCCCCCGAT CCTCCTGTTTAACATTCTGGGACTGGTCCAGGCTTGGAAAAGCAAAAAGACACCCATGGGCTTTAGCTATGACACAAGGTGTTTCGATAGCACAGTGA GACTATATGTTTGCCCCTACCCTCTGGGCTAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAAGCCCCTCAG CGTCATCCCTACCTCCGGCGATGTGGTCGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGATTTCGATAGCGTCATCGATTGCCATAGCA AAAAGAAATGCGATGAGCTCGCCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCTCGACGTCGTGCTCCCCTGTAGCTTT ACCACACTGCCTGCCCTCAGCACAGGCCTCATCCATCTGCATCAGAATATCGTCGACGTCCAGTATCTGTATAAAGGGAAGGTGGCGTGCCTGGCGCTGT GTATGCCCTCTACGGAATGTGGCCCCTCCTGCTCCTGCTCCTGCCTCTGCCTCAGAGAGCCCTATAGCCCTATCACATACTCCACCTATGGCAAATTCC TCGCCGATGGCGGATGCTCCGGCGGAGCCTATGACATTATCATTTGCGATGAGTGTCCCAGAAGCGTCAGGGCTAGGCTCCTGGCTAGGGGAGGCAGA GCCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAAAAGGCTGTGGCTCACATTAACTCCGTGTGGAAGGATCTGCTCGAGGATAG $\tt CGTCACCCCTATCGATACCACAATCATGGCCAAAAACGAATTCACACCCTCCCCCGTCGTCGTCGCCACAACCGATACGTCCGGCGCTCCCCACATACT$ CCTGGGGAGCCAATGACACAGACGTCTTCGTCCCCGGATGCGTCCCCTGTGTGAGAGAGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCACA GTGGCTACCAGAGACGGAAAGCTCCAGGATTGCACAATGCTCGTGTGTGGGGGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGC GAGCTCACCCCTGCCGAAACCACAGTGAGACTGAGAGCCTATATGAATACCCCTGGCCTCCCCGTCTGCCAAGACCATCTGGAATTCTGGCCCCAACC CGANTACGATCTGGAACTGATTACCTCCTGCTCCAGCAATGTCTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTATCTGGGAAAGGTCATCG ATACCCTCACCTGTGGCTTTGCCGATCTGATGGGCTATATCCCTCTGGTCGGCGCTCCCCTCGGCGGAGCCGCTGCCATTCCCCTCGAGGTCATCAAA ggcggaaggcatctgattttctgtcactccaagaaaaagtgtgacgaactggccaaactggtcggcgagtgctcgccgctctggctgtttt CCTCAGCACAGGCTGTGTGGCCAGAATCGTCCTGTCCGGCAAACCCGCTTGCGAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGA AGCCATGCCAGACCCAGATGGTTTTGGTTTTGCCTCCTGCTCAGCTCCAGCACAAGCGGAATCACAGGCGGATAACACCACAAGCTCCGAGCCTGC CCCTAGCGGATGCCCTCCCGATAGCGATGCCGAAAGGACACAGAGAAGGGGGAAGGGACAGGCAAACCCGGAATCTATAGGTTTGTGGCTCCCG GACCTCGAGGATAGGGATGAGGCTCAGCTCCACGTCTGGGTCCCCCCTCTGAATGTGAGAGGGGGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGT GCATCCCACACTGGGAGTGAGAGCCACAAGGAAAACCTCCGAGAGAAGCCAACCCAGAGGCAACCCATTCCCAAAGCCAGAAGGCCTGAGG GAAACGTCAGCGTCGCCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCCTACCACACCCCCTCGCCAGAGCCGCTTGGGAAAGCGAA $\tt CCCGCTCCCTGCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGGCGAACCCGGAGACCCTATCGGAGGCCATTA$ CGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATCTGACACCCCTCAGGGATCCCTCCACGGAAGACCTCGTGA ATCTGCTCCCCGCTATCCTCAGCCCTGGCGCTCTGGTCGTGGGAGTGGTCTGCGCTGCCATTCTGAGAATCCTCGACATGATCGCTGGCGCTCACTGG GGGAAGCAGACCCTCCTGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAATTGGACAACCCAAGGCTGTAACTGTAGCATTTACCCTGGCCATATCA

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TCAGGGTCTGCGAAAAGATGATGGGATACATTCCCCTCGTGGGAGCCCCTCTGGGGAGGCGCTGCCAGAGCCCTCGCCCATGGCGTCAGGGTCCTGGAA GACGGAGTGAATGGCGGAAACGCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCCGGAGCCAAACAGAATATCCAACTGATTAACACAAA CGGACTGGCTCTGCCTCAGCTGTCTGACAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAAACGATTGCCCTGGCA GAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACACGCCGCTCAGACATTCCTCGCCACATGCATTAACGGAGTGTGTCCCGCTACCCAA CTGAGAAGGCATATCGATCTGCTCGTGGGAAGCGCTACCCTCTGCTCCGCCCTCTACGTCGGCGATCTGTGTGGCTCCCACGCCTCCCACAGGCTCCGG GGCCCCTCTACGGAAACGAAGGCTGTGGCTGGGCCGGATGGCTCCTGTCCCCCAGAGGCTCCACCGAAGACGTCGTGTTGCTCCATGTCCTACTCC TGGACAGGCGCTCTGGTCACCCCTTGCGCTGCCGAAGAGCAAAAGCTCCCCATTGCCCTCGACACAGAGGTCGCCGCTAGCTGTCGCCGAAGAGCTCCT TTGGCGGAGCCGGAAACAATACCCTCCACTGTCCCACAAGCGTCGAGGAAGCCTGTAGCCTCACCCCTCCGCATAGCGCTAAGTCCAAGTTTGGCTAT GGCTTTCACAGCCGCTGTGACACAGATTGTGGGAGGCGTCTACCTCCTGCCTAGGAGAGGCCCTAGGCTCCGGCGTCAGGGCTACCAGAAAGACAAGCG AAAGGTCCCAGCCTCTGCATAGCTATAGCCCTGGCGAAATCAATAGGGTCGCCGCTTGCCTCAGGAAACTGGGAGTGCCTCCCCTCAGGGCTTGGAGA GAATCTGGAAACCACAATGAGAAGCCCTGTGTTTACCGATAACTCCAGCCCTCCCGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTCGCCACACCCC CTGGCTCCGTGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAACTGGTCTTCGATATCACA AAGCTCCTGCTCGCCGTCTTCGGACCCCTTGGATTCTGCAAGCCTCCCTGCTCAAGGTCCCCTATTTCGTCACCGCTGCCCTCGTGATGGCCCAACT CCCTGGATCCCACACTCCACAATCGAAACCACAACCCTCCCCCAAGACGCTGTGTCCCACGGACCCCACACCCCTCCTGTATAGGCTCGGCGCTGTGCAA AACGAAGTGACACTGACACCCCTGTGACAAAGTATATCATGACCTGTGCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACCGCGGCGGACC CCTCACCAATAGCAGAGGCGAAAACTGTGGGTATAGGAGATGCGTCATCGGAGGCGCTGGCAATAACACACTGCATTGCCCTACCGATTGCTTTAGGA GGCGATAGCAGAGGCTCCCTGCTCAACATGTGGTCCGGCACATTCCCTATCAATGCCTATACCACGGCCCTTGCACACCCCCTCCCGGCTCCCAATTA CACATTCGCTCTGTGGCACTCCACCGATGCCACAAGCATTCTGGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTGC TCGCCACATACGTCCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCCAACTGCTCAGGAGACTGCATCAGTGG AGGCCTAGCTGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACACTGACATGCGGATTCGCTGACCTCGGCCCTGA ATCTGCCTTACATTGAGCAAGGCATGATGCTCGCCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACATACCAAGCCACAGTGTGTGCCAGA GCCCAAGCCCCTCCCCCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTCTGCGGGAATCGTCCCGCCTAAGTCCGTGTGTGG GAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGGATGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTAC CCCTCTGCTCTACAGACTGGGAGCCGTCCAGAATCTGGCTGAGCAATTCAAACAGAAAGCCCTCGGCCTCCTGCAAACCGCTAGCAGACAGGCTGAGG TCATCGCTCCCGCTGTGCAAACCAATTGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACGTGTGGAATTCATTAGCGGGAATCCAATACCTCGCCGGA CTGTCCACCCTCCCGGACTGATTGCCTTTGCCTCCAGGGGAAACCATGTGTCCCCCACACACTATGTGCCTGAGTCCGACGCCGCCGAGGGTCAC GTGGCTGCCCAACTGGCTGCCCTGGCGCTGCCACAGCCTTTGTGGGAGCCGGACTGGCTGCCGTTGGCTGCCACTTGGCACATTAA $\tt CTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACACAAATTCAATAACGCTCTGTCCCAACTCCCTGC$ AGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAGACGTCAAGTTTCCCGGAGGCGGAAGCCAAACCAAACAGTCCGGCGAAAACTTTCCCTATCT TCAACAATACCAGACCCCCTCTGGGAAACTGGTTCGGATGCACAGTGCCTCCCCCTAGGAAAAAGAGAACCGTCGTGCTCACCGAAAGCACACTGTCC ACCECTCTGGCTGAGCTCGCCACAAAGTCCTTCGGAAGCACAACCTCCAGGTCCGCCTGTCAGAGAAAAAAGGTCACCTTTGACAGACTGCAAGT GCTCGACTCCCACTATCAGGATGTGCTCGACCAAGCCGAAACCGCTGGCGCTAGGCTCGTGGTCCTGGCTACCGCTACCCCTCCCGGAAGCGTCACCG CTCCGCCTCCAGGCAAGCCGAAGTGATTGCCCCTGCCGTCCAGACAAACTGGCAGAAACTGGAAGTGTTTTGGGCTAAGCATATGTGGAACTTTTGCA GAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAAAGCCAGAGCCGCTTGCAGAGCCGCTGGCCTCTTCGATAGGCTC CAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAGAGGTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTCGGCCCTCTGACAAACTCCAG GGGAGAGAATTGCGGATACAGAAGGTGTAGGGGTAGCGGAGTGCTCACCACAAGCTGTGGCAATACCCTCATCATGCACACAAGGTGTCACTGTGGCG CTGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGAGAGGGTCAGCTTTAGGGTCGGCCTCCACGAATACCCT GTGGGAAGCCAACTGCCTTGCGAACCCGAACCCGATGTGGCTGTGCTCACCTCCAAGGAAGTGAAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCT AGCCCTCCATGGCTAGCTCCAGCGCTAGCCCTAGGCCTATCTCCTACCTCAAGGGAAGCTCCGGCGGACCCCTCCTGTGCCCATGCCCATGC $\tt CGTCGGCATTTTCAGAGCCGCTGACTTTGACCAAGGCTGGGGCCCTATCTCCTACGCTAACGGAAGCGGACCCGATCAGAGACCCTATTGCTGGCACT$ ATCCCCCTAAGCCTAGGCATGTGGGACCCGGGAGGGGACCCGTCCAGTGGATGAATAGGCTCATCGCTTTCGCTAGCAGAGGCAATCACGTCAGCCCT ACCCATTGCCTCTGGATGATGCTCCTGATTAGCCCAAGCCGAAGCCGCTCTGGAAAACCTCGTGATTCTGAATGCCGCTAGCCTCGCCGGAACCCCATAT CATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAGAGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATGCTGATTCACC TCCACCAAAACATTGTGGATGTGCAATACCTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTATGTGTCCCACGCTAGGCCT AGGTGGTTCTGGTTCTGCTCCTCGCCGCTGGCGTCGGCATTTACCTCCTGCCTAACAGAGCCGCTGCCGCTACCGCTTTGGCGCTTTA CATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAAACCGGAAGGGTCCAGGGACTGCTCAGGATTTGCGCTCTGG CTAGGAAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGCTAGGAGATTCGCTCAGGCTCTGCCTGTGTGGGCCCAGACCCGAT TACAATCCCCCTCTGGTCGAGACATGGAAAAAGCCTGACTATGAGCCTACCGCTGCCCAAACCTTTCTGGCTACCTGTATCAATGGCGTCTGCTGGAC CGTCTACCATGGCGCTGGCACAAGGACAATCGCTAGGCCTTGGGCTCACAATGGCCTCGGGGATCTGGCTGTGGCTGGAACCCGTGTTTTAGCC AAATGGAAACCAAACTGATTACCTGGGGCGCTAAGGGACCCGTCATCCAAATGTATACCAATGTGGATCAGGATCTGGTCGGCTGGCCCGCTCCCCAA GATTCTGAGAAAGTCCCTGACAGGCACATACGTCTACAATCACCTCACCCCTCTGAGAGACTGGGCCCATAACGGACTGAGAGACCTCGCCGTCGCCG TCGAGCCTGTGTGTACCAGAGGCGTCGCCAAAGCCGTCGACTTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAAT GCCCTCGGCATTAACGCTGTGGCTTACTATAGGGGACTGGATGTCTCCGTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGATATGTCCGC

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CGATCTGGAAGTGGTCACCTCCACCTGGGTGCTCGTGGGAGGCGTCCTGGCTGCCCTCGCCGCTTACTGTCCACCGGAGCCCTCATGACAGGCTATACCGGAGACTTTGACTCCGTGATTGACTGTAACACATGCGTCACCCCAAACCGTCGACTTTAGCCTCGACCCTAACACAAACAGAAGGCCTCAGGAT GTGAAATTCCCTGGCGGAGGCCAAATCGTCGGCGGAGTGTATCTGCTCCCCAGAAGGGGACCCAGAAGGGCTCTGGCTCACGGAGTGAGAGTGCTCGA CGATGGCGTCAACTATGCCACAGGCAATCTGCCTGGCTGTAGCTTTAGCATTTTCCTCAGCAAATTCGGATACGGAGCCAAAGACGTCAGGTGTCACG CTAGGAAAGCCGTCGCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAAACCCCTGGCGCTAAGCAAAACATTCAGCTCATCAATACCAATGGCTCC ${\tt CCCTGAGAGACTGGCTAGCTGTAGGAGACTGACAGTGGTCCTGCTCTTCCTCCTGCCGGATGCCAGAGTGTGTAGCTGTCTGGATGATGCTGC}$ TCATCTCCCAGGCTGAGGCTGCCCTCGACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCCTCGACCTCCCCCCTATCATCAGAGACTGCAT GGCCTCAGCGCTTTCTCCTCGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCAAAGGCCCTGTGATTCAGATGTACACAAACGTCGA CCAAGACCTCTACAGATTCGTCGCCCCTGGCGAAAGGCCTAGCGGAATGTTTGACTCCAGCGTCCTGTGTGAGTGTTACGATGCCGGATGCGCTTGGT ATAGGTCCGAGCTCAGCCCTCTGCTCCACCACACAGTGGCAGGTCCTGCCTTGCTCCTTCACAACCCTCCCCGGCTCTGTCCACCGGACTGAGA AAGCTCGGCGTCCCCCTCTGAGAGCCTGGAGGCATAGGGCTAGGTCCGTGAGAGGCCAGACTGCTCGCCAGAGGCGGAAGGGCTAGCCCTCTGACAAC CTCCCAGACACTGCTCTTCAATATCCTCGGCGGATGGGTCGCCGCTCAGCTCGCGGAGCCGCTACCGCTTGTGGATCCTCCAGGCTAGCC TCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATGGTGAAAAACCGAACCATGAGGATTGTGGGA CCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGGGGGGGTCGCCCTCAGCACAACCGGAGAGATTCCCTTTTA CGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGACACCTCATCTTTCTGACAAGGGATCCCACAACCCCTCTGGGTAGGGCTGCCTGGGAGA CAGCCAGACACACCCCGTCAACTCCTGGCTCGGCAATATCATTAGGGTCAGCGCTGAGGAATACGTCGAGATTAGGAGAGTGGGAGACTTTCACTAT GTGACAGGCATGACCACAGACAATCTGAAATGCCCTCCCGTCGTGCATGGCTGTCCCCCTCCCCAGAAGCCCCTCCCGTCCCCTCCCAGAAA GAAAAGGACAGTGGTCCTGACAGAGTCCACCCTCAGCACAGCCCTCGCCGAACTGGCTACCAAAAGCTTTGGCTCCAGCTCCACCTCCGGCATTACCG GAGACAATACCACAACCTCCGTGTCCTGCCAAAGGGGATACAAAGGCGTCTGGAGAGGCGATGGCATTATGCATACCAGATGCCATTGCGGAGCCGAA ATCACAGGCCATGTGTTTCTGGTCGGCCAACTGTTTACCTTTAGCCCCTAGGAGACACTGGACCACAGGGGATGCAACTTGCTCCATCTATCCCGGACA CATTTTCGTCGGCGCTGGCCTGGCCGGAGCCGCTATCGGAAGCGTCGGCCTAAAGTGCTCGTCGGATATCCTCGCCGGATACGGAGCCGGAGACA TTTGGGATTGGATTTGGGAAGTGCTCAGCGATTTCAAAACCTGGCTGAAAGCCCAAACTGATGCCCCAACTGCCATTCCCTTTAACTCCAGCATT GTGTATGAGGCTGCCGATGCCATTCTGCATACCCCTGGCTGTGCCTTGCGTCAGGGAAGGCAATGCCTCCAGGTGTAGCTCCGGCTGTCCCGAAAG GCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGGATGGGGACCCATTAGCTATGCCAATGGCTCCAGGACAGAGGGAAGCCATTTACCAATGCT GTGACCTCGACCCTCAGGCTAGGGTCGCCATTAAGTCCCTGACAGAGAGACTGTATGTGGGAGTGTCCAAGGGATGGAGACTGCTCGCCCCTATCACA GCCTATGCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCCTGACATTCTTTAGCGTCCTGATTGCCAGAGACCAACTGGAACAGGCTCT GGATTGCGAAATCTATGGCGCTTGCTATAGCATTGAGCCTCTGGATTGCCAAGTGCCTTAGCCCTGAGTTTTTCACAGAGCTCGACGGAGTGAGACTGC ATAGGTTTGCCCCTCCTGTAAGCCTCTGCTCAGGGAAACCTGTTACATTAAGGCTAGGGCTGCCTGTAGGGCTGCCGGACTGCAAGACTGTACCATG CTGGTCTGCGGAGACGATCTGGTCGTGATTATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATA CAACCCAATGGCAAACCGGACACAGAATGGCTTGGGATATGATGATGATTGGTCCCCCACAGCCGCTCTGGTCATGGCTCAGGCTCCTGAGAATCCCT CGATAGCCCTGACGCTGAGCTCATCGAAGCCAATCTGCTCTGGAGACAGGAAATGGGAGGCAATATCACAAGGGTCGAGTCCGAGAATGAGGGAGTGT $\tt ATCCCTAAGGCTAGGAGCCCGAAGGCAGAACCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAATCTGATTGTGTTTCCCGATCTGGGAGT$ GAGAGTGTGTGAGAAAATGGCTCTGTATGACGTCGTGTCCAAGCTCCCCCTCGCCGTCATGGGATACGCTACCGGAAACCTCCCCGGATGCTCCTTCT GGCGTCGCCCGGAGCCCTCCTGGCTTTCAAAATCATGAGCGGAGAGGTCAGCTATAGCTCCATGCCTCCCCTCGAGGGAGAGCCTGGCGATCCCGATCT GTCCGACGGAAGCTGGAGCACAGTGTCCAGCGAAGCCGGAAGGCAAGAGATGGCCGGAAACATTACCAGAGTGGAAAGCGAAAACAAAGTGGTCATCC TACCTCGTGACAAGGCATGCCGATGGCTGTAGCGGAGGCGCTTACGATATCATTATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGG CATTGGCACAGTGCTCACCTTTACCATTGAGACAACCACACTGCCTCAGGATGCCGTCAGCAGAACCCAAAGGAGAGCCAGAACCGGAAAGGGGAAAGC CTGGCATTGACTGTTTCAGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTCGACTATCCCTAT CTGCCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCCGCCTCGTGACACCCTGTGCCGCTGAGGAACAGAAACTGCCTTATCAATGCCCT CAGCAATAGCCTCCTGAGACACCATAACCTCGTGTATATCTCCAGCGAATGCACAACCCCTTGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGGA TCTGTGAGGTCCTGTCCGACTTTAAGACATGGCTCAAGGCTCATGCCTCAGCTCCCCGGAATCCCTTTCGTCAGCTGTCAGAGAGGCTATAAG GGAGTGTGGAGGGGAGACGGAAGCGGACCCTGGATCACACCCAGATGCCTCGTGGATTACCCTTACAGACTGTGGCACTATCCCTGTACCATTAACTA TACCATTTTCAAA

HepC Savine Cassette Sequences (A+B+C) with specific restriction sites removed which can be joined to generate a single expressible open reading frame that encodes the hepc Savine protein above

Cassette A

145/216

CTGGCCTATCAAATGGGAATACGTCGTGCTCCTGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCCCTGAATAACACAA GGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCTTTC ACAGAGGCTATGACAAGGTATAGCGCTCCCCTGGCGATCCCCCTCAGCCTGAGTATGACCTCGAGCTCATCACAAGCTG GCGGAGGCGTCGTGCTCCAGCAAACCAGAGGCCTCCTGGGATGCATTATCACAAGCCTCACCGGAAGGGATAAGAATCAG GTCGAGGGAGAGGTCCAGATTGTGTCCAGCTCCCCCCTGCCGTCCCCCAAAGCTTTCAGGTCGCCCATCTGCATGCCCC TACCGGAAGCGGAAAGTCCACCAAAGTGCCTGCCGCTAACACACCCGGACTGCCTGTGTGTCAGGATCACCTCGAGTTTT GGGAAGCCTCTCACAGGCCTCACCCATATCGATGCCCATTTCCTCGTGCTCCTGCTCTTCGCTGGCGTgGAtGCTGAG ACACACGTCACCGGAGGCAATGCCGGAAGGACAACCTCCGGCCTCGTGTCCCTGAGGTCACCCTCACCCATCCCGT CACCAAATACATTATGACATGCATGAGGGCTGACCTCGAGGTCGTGACAAGCACATGGGTCCTGGTCGTGGGACTGATGG CCCTCACCCTCAGCCCTTACTATAAGAGATACATTAGCTGGTGGCTCGCTGGTGGCTGCAATACTTTCTGACAAGGGTCGCC ATTTGGGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGACTGGA TCTGTCCATCGCTTACTTTAGCATGGTGGGAAACTGGGCCAAAGTGCTCGTGGTCCTGCTCTGTTTGCCGGAGTGGATG CCGAAACCCATGTGACAAGGCTCGCCAGAGGCTCCCCCCTAGCATGGCTCCAGCTCCGCCTCCCAGCTCAGCGCTCCC ATGGGTCCCGGGGCCGTCTACGCTCTGTATGGCATGCAGCTCCCCTGTGAGCCTGAGCCTGACGTCGCCGTCCTGACAA GCATGCTGACAGACCCTAGCCATATCACAGCCGAAGCCGCTGGCAGAGACTCCGTGACACCCATTGACACAACCATTATG GCTAAGAATGAGGTCTTCTGTGTGCAACCCGAAAAGGGGGGGCAGAAAGCCTGCCAGATACGCTGCCCAAGGCTATAAGGT CCTGGTCCTGAATCCCTCCGTGGCTGCCACACTGGGATTCGGAGCCTATATGTCCAAGGCTCACGGAGTGAGAAACTCCA CCGGACTGTATCACGTCACCAATGACTGTCCCAATAGCTCCATCGTCTACGAAGCCGCTGACGCTATCCTCCACACAAGC TCCTACGGATTCCAATACTCCCCGGGACAGAGAGTGGAGTTLCTCGTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGG GCCCTGCCGATGGCATGAGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTACCGCTAACCATGACTCCCCCGATGCC GAACTGATTGAGGCTAACCTCCTGTGGAACCCTGCCATTGCCTCCCTGATGGCCTTTACCGCTGCCGTCACCTCCCCCCT CACCACAAGCCAAACCCTCCTGTTTAACATTCTGGGACTGGTCCAGGCTTGGAAAAGGCAAAAAGACACCCATGGGCTTTA CTCAGGAAAAGCAGAAGGTTTGCCCAAGCCCTCCCGTCTGGGCTAGGCCTGACTATATGTTTGCCCCCTACCCTCTGGGC TAGGATGATCCTCATGACACACTTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAAGCCCTCAGCGTCATCCCTA CCTCCGGCGATGTGGTCGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGATTTCGATAGCGTCATCGATTGC CATAGCAAAAAGAAATGCGATGAGCTCGCCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCT ALGTCCAGTATCTGTATAAGGGAAGGTGGGTGCCTGGCGCTGTGTATGCCCTCTACGGAATGTGGCCCCTCCTGCTCCTG CTCCTGGCTCTGCCTCAGAGAGCCTATAGCCCTATCACATACTCCACCTATGGCAAATTCCTCGCCGATGGCGGATGCTC CGGCGGAGCCTATGACATTATCATTTGCGATGAGTGTGCCAGAAGCGTCAGGGCTAGGCTCCTGGCTAGGGGAGGCAGAG ${\tt CCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAAAAGGCTGTGGCTCACATTAACTCCGTGTGGAAG}$ GATCTGCTCGAGGATAGCGTCACCCCTATCGATACCACAATCATGGCCAAAAACGAGTTtACACCCTCCCCGTCGTCGT CGGCACAACCGATAGGTCCGGCGCTCCCACATACTCCTGGGGAGCCAATGACACAGACGTCTTCGTCCCCGGATGCGTCC CCTGTGTGAGAGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCACAGTGGCTACCAGAGACGGAAAGCTCCAG GATTGCACAATGCTCGTGTGTGGCGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCGCTAGCCT CAGGGCTGTGGCTGCTCTGGTCGCCTTTAAGATTATGTCCGGCGAAGTGCCTAGCACAGAGGATCTGGTCAACCTCC TGCCTGCCATTCTGTCCTACGATACCAGATGCTTTGACTCCACCGTCACCGAAAGCGATATCAGAACCGAAGAGGCTATC TATCAGTGTGCGATCTcGAcCCCCAAGAGCTCACCCCTGCCGAAACCACAGTGAGACTGAGAGCCTATATGAATACCCC TGGCCTCCCGTCTGCCAAGACCATCTGGAqTTLTGGCCCCAACCCGAATACGATCTGGAACTGATTACCTCCTCCTCCA GCAATGTGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTATCTGGGAAAGGTCATCGATACCCTCACCTGTGGC TTTGCCGATCTGATGGGCTATATCCCTCTGGTCGGCGGCTCCCCTCGGCGGAGCCGCTGCCATTCCCCTCGAGGTCATCAA AGGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAAGTGTGACGAACTTGGCTGCCAAACTTGGTCGGCGGAGTGCTCC CCGCTCTGGCTGCCTATTGCCTCAGCACAGGCTGTGTGGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCTTGC GAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCTGAGAGCCTTTACCGAAGCCATGACCAGATACTCCGCCCTTCCCGG AGACCCTGGCTGGTTCACAGCCGGATACTCCGGCGGAGACATTTACCATAGCGTCAGCCCAGACCCAGACCCAGATGGTTTT GGTTTTGCCTCCTGCTCAGCTCCAGCACAAGCGGAATCACAGGCGGATAACACAACCACAAGCTCCGAGCCTGCCCCTAGC GGATGCCCTCCGGATAGCGATGCCGAAAGGACACAGAGAAGGGCAAGGACAGGCAGAGGCAAACCCGGAATCTATAGGTT CCTGTAACTGGACCAGAGGCGAAAGGTGTGACCTCGAGGGATGAGGCTCAGGCTCCACGTCTGGGTCCCCCCTCTG AATGTGAGAGGCGGAAGGGATGCCGTCATCCTCGTGATGTGCGTCGTGCATCCCACACTGGGAGTGAGAGCCACAAGGAA AACCTCCGAGAGAGCCAACCCAGAGGCAGAAGGCAACCCATTCCCAAAGCCAGAAGGCCTGAGGGAAACGTCAGCGTCG CCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCTACCACCACCCCTCGCCAGAGCCGCTTGGGAAAGC GAACCCGCTCCCTCGGCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGGCGAACCCGG AGACCCTATCGGAGGCCATTACGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATC TGACACCCTTCAGAGACCCCTCCACCGAAGACCTCGTGAATCTGCTCCCCGCTATCCTCAGCCCTGGCGCTCTGGTCGTG GGAGTGGTCTGCGCTGCCATTCTGAGAATCCTCGACATGATCGCTGGCGCTCACTGGGGGGGTCCTGGCTTGCCTA GCAGACCCTCCTGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAATgtcgactgagaattcgcc

Cassette B

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GCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCCGGAGCCAAACAGAATATCCAACTGATTAACACAAACGG ACTGGCTCTGCTCAGCTGTCTGACAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAA ACGATTGCCTGGCAGAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACAGCCGCTCAGACATTCCTCGCC ACATGCATTAACGGAGTGTCCCCGCTACCCAACTGAGAAGGCATATCGATCTGCTCGTGGGAAGCGCTACCCTCTGCTC CGCCCTCTACGTCGGCGATCTGTGGGCTCCCACGCTCCCACAGGCTCCGGCAAAAGCACAAAGGTCCCCGCTGCCTATG CCGCTCAGGGATACAAAGTGCTCGTGCTCAACCCTAGCGTCAGGACATGGGCTCAGCCTGGCCTATCCCTGGCCCCTCTAC GGAAACGAAGGCTGTGGCTGGGCCGGATGGCTCCTGTCCCCCAGAGGCTCCACCGAAGACGTCGTGTTGCTCCATGTC CTACTCCTGGACAGGCGCTCTGGTCACCCCTTGCGCTGCCGAAGAGCCAAAAGCTCCCCATTGCCCTCGACACAGAGGTCG CCGCTAGCTGTGGCGGAGTGGTCCTGGTCGGCCTCATGGCTCTGACACTGTCCCCCTATTACAAAAGGTATTGGATGAAC AAGCGTCGAGGAAGCCTGTAGCCTCACCCCCCCCCATAGCGCTAAGTCCAAGTTTGGCTATGGCGCTAAGGATGTGAGAT GCCATGCCAGAATCTCCGGCATTCAGTATCTGGCTGGCCTCAGCACACTGCCTGGCAATCCCGCTATCGCTAGCCTCATG GCTTTCACAGCCGCTGTGACACAGATTGTGGGAGGCGTCTACCTCCTGCCTAGGAGAGGCCCCTAGGCTCGGCGTCAGGGC TACCAGAAAGACAAGCGAAAGGTCCCAGCCTCTGCATAGCTATAGCCCTGGCGAAATCAATAGGGTCGCCGCTTGCCTCA GGAAACTGGGAGTGCCTCCCCTCAGGGCTTGGAGACACAGAACCGCTAGGCATACCCCTGTGAATAGCTGGGCAGAAC ATTATCATGTTCGCTCCCACACTGTGGGCCAGAATGATTCTGATGACCCATGAGAATCTGGAAACCACAATGAGAAGCCC TGTGTTTACCGATAACTCCAGCCCTCCGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTCGCCACACCCCCTGGCTCCG TGACAGTGCCTCACCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGGGAAATCCCTTTCTATGGCAAACTGGTCTTC GATATCACAAAGCTCCTGCTCGCCGTCTTCGGACCCCTCTGGATTCTGCAAGCCTCCCTGCTCAAGGTCCCCTATTTCGT CACCGCTGCCCTCGTGATGGCCCAACTGCTCAGGATTCCCCAAGCCATTCTGGATATGATTGCCGGAGCCCATTGGGGAG TGCTCGCCGGATGCAATACCTGTGTGACACAGACGGGGTTTCTCCCTcGAcCCCACATTCACAATCGAAACCACAACC CTCCCCCAAGACGCTGTGTCCCCACGGACCCACACCCCTCCTGTATAGGCTCGGCGCTGTGCAAAACGAAGTGACACTGAC ACACCCTGTGACAAAGTATATCATGACCTGTGCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGAC CCCTCACCAATAGCAGAGGCGAAAACTGTGGCTATAGGAGATGCGTCATCGGAGGGGCGCTGCCAATAACACTGCATTGC CCTACCGATGCTTTAGGAAACACCCTGAGGCTACCTATAGCAGATGCGGAACCTGTGGCTCCAGCGATCTGTATCTGGT CACCAGACACGCTGACGTCATCCCTGTGAGAAGGAGGGGGATAGCAGAGGCTCCCTGCTCAACATGTGGTCCGGCACAT TCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCTCCCGCTCCCAATTACACATTCGCTCTGTGGCACTCCACC GATGCCACAAGCATTCTGGGAATCGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTCGTCGCCAC ATACGTCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCCAACTGCTCAGGAGAC TGCATCAGTGGAGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGGAGGAGAACCTCGGCAAAGTGATTGACACACTG ACATGOGGATTOGCTGACCTGGCCCTGACCAAAGGCCTTACTGTTGGCATTACCCTCCCAAACCCTGTGGCATTGTGCC TGCCAAAAGCGTCTGCGGACCCGTCTACTGTGAGGAATGCTCCCAGCATCTGCCTTACATTGAGCAAGGCATGATGCTCG CCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACATACCAAGCCACAGTGTGTGCCAGAGCCCAAGCCCCTCCC CCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTCTGCGGAATCGTCCCCGCTAAGTCCGTGTG GATGGCTCCTGGTCCACCGTCAGCTCCGAGGCTGGCACAGAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGG ATGGGATCAGAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTACCCCTCTGCTCTACAGACTGGGAG CCGTCCAGAATCTGGCTGAGCAATTCAAACAGAAAGCCCTCGGCCTCGCAAACCGCTAGCAGACAGGCTGAGGTCATC GCTCCCGCTGTGCAAACCAATTGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTTCATTAGCGGAATCCA ATACCTCGCCGGACTGTCCACCCTCCCGGACTGATTGCCTTTGCCTCCAGGGGAAACCATGTGTCCCCCACACACTATG TGCCTGAGTCCGACGCTGCCGCTAGCGCTATCCTCGCCACACTGTGTAGCGCTCTGTATGTGGGAGACCTCTGC GGAAGCGTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGCATAGCTCCGTGCTCTGCGAATGCTATGACGC TGGCTGTGCCTGGTACGAACTGACACCCGCTGAGACAACCGTCAGGCTTACATGGGCTGGGTGGCTGCCCAAC ATTAACTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACAAATTCAA TAACGCTCTGTCCAACTCCCTGCTCAGGCATCACAATCTGGTCTACTCCACCACAAGCAGAAGCGCTTGCCAAAGGCAAA AGAAAGTGACAGCCGCTATGTCCACCAATCCCAAACCCCAAAGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAGAC GTCAAGTTTCCCGGAGGCGGAAGCCAAACCAAACAGTCCGGCGAAAACTTTCCCTATCTGGTCGCCTATCAGGCTACCGT ACAATACCAGACCCCTCTGGGAAACTGGTTCGGATGCACAGTGCCTCCCCTAGGAAAAAGAGAAACCGTCGTGCTCACC GAAAGCACACTGTCCACCGCTCTGGCTGAGCTCGCCACAAAGTCCTTCGGAAGCACAACCTCCAGGTCCGCCTGTCAGAG ACAGAAAAAGGTCACCTTGACAGACTGCAAGTGCTCGACTCCCACTATCAGGATGTGCTCGACCAAGCCGAAACCGCTG GCGCTAGGCTCGTGGTCCTGGCTACCGCTACCCCTCCCGGAAGCGTCACCGTCCCCCATCCCAATATCGAqTTtCATTAC GTCACCGGAATGACAACCGATAACCTCAAGTGTCCCTGTCAGGTCCCCTCCCCCGAGTT+TTTACCGAACTGGATGGCGT CCTGAAACTGACACCCATTGCCGCTGCCGGAAGGCTCGACCTCAGCCGGATGGTTTACCGCTGGCTATAGCCGGAGGCGATA TCTATCACTCCGCCTCCAGGCAAGCCGAAGTGATTGCCCCTGCCGTCCAGACAACTGGCAGAACTGGCAGAACTGTTTTGG GCTAAGCATATGTGGAACTTTTGCAGAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAA ASCCAGAGCCGCTTGCAGAGCCGCTCGCCTCTTCGATAGGCTCCAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAG AGGTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTCGGCCCTCTGACAAACTCCAGGGGAGAAATTGCGGATAC TGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGAGAGGGTCAGCTTTAGGGTCG GCCTCCACGAATACCCTGTGGGAAGCCAACTGCCTTGCGAACCCGAACCCGATGTGGCTGTGCTCACCTCCAAGGAAGTG AAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCTGTCCGTGGAAGAGGGCTTGCTCCCTGACACCCCCTCACTCCGCCAA AGGCAGAGACGCTGTGATTCTGCTCATGTGTGGGTCCACCCTACCCTCGTGTTTGACATTACCAAACTGCTCCTGGCTG TGTTTGGCCCTATGCTCACCGATCCCTCCCACATTACCGCTGAGGCTGCCGGAAGGAGACTGGCTAGGGGAAGCCCTCCC TCCATGGCTAGCTCCAGCGCTAGCCCTAGGCCTATCTCCTACCTCAAGGGAAGCTCCGGCGGACCCCTCCTGTGTCCCGC TGGCCATGCCGTCGGCATTTTCAGAGCCGCTGACTTTGACCAAGGCTGGGGCCCTATCTCCTACGCTAAGCGGAAGCGGAC AATAGGCTCATCGCTTTCGCTAGCAGAGGCAATCACGTCAGCCCTACCCATctcgagtgagaattcgcc

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Cassette C

ggcggatccaccatgctcgagTGCCTCTGGATGATGCTCCTGATTAGCCAAGCCGAAGCCGCTCTGGAAAACCTCGTGAT TCTGAATGCCGCTAGCCTCGCCGGAACCCATATCATTCCCGATAGGGAAGTGCTCTACAGGAGGTTTTGACGAAATGGAAG AGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATGCTGATTCACCTCCACCAAAACATTGTGGATGTGCAATAC $\tt CTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTATGTGTCCCACGCTAGGCCTAGGTGGTTCTG$ GTTCTGTCTGCTCGCCGCTGGCGTCGGCATTTACCTCCTCCTAACAGAGCCGCTGCCGCTACCCTCGGCTTTG GCGCTTACATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGAAGGGTCCAG GGACTGCTCAGGATTTGCGCTCTGGCTAGGAAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGC TAGGAGATTCGCTCAGGCTCTGCCTGTGGGCCAGACCCGATTACAATCCCCCTCTGGTCGAGACATCGAAAAAGCCTG ACTATGAGCCTACCGCTGCCCAAACCTTTCTGGCTACCTGTATCAATGGCGTCTGCTGGACCGTCTACCATGGCGCTGGC ACAAGGACAATCGCTAGCCCTTGGGCTCACAATGGCCTCAGGGATCTGGCTGTGGCTGTGGAACCCGTCGTGTTTAGCCA AATGGAAACCAAACTGATTACCTGGGGCGCTAAGGGACCCGTCATCCAAATGTATACCAATGTGGATCAGGATCTGGTCG GCTGGCCCGCTCCCCAAGGCTCCAGGTCCCTGACACCCTGTAAGGTCGTGATTCTGGATAGCTTTTGACCCTCTGGTCGCC GAAGAGGATGAGAGAGAGATTAGCGTCCCCGCTGAGAATCTCTGAGAAAGTCCCTGACAGGCACATACGTCTACAATCACCT CACCCTCTGAGAGACTGGGCCCATAACGGACTGAGAGACCTCGCCGTCGCCGTCGAGCCTGTGTGTACCAGAGGCGTCG CCAAAGCCGTgGAtTTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAATGCCCTCGGC ATTAACGCTGTGGCTTACTATAGGGGACTCGATGTCCCTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGA TATGTCCGCCGATCTGGAAGTGGTCACCTCCACCTGGGTGCTCGTGGGAGGCGTCCTGGCTGCCGCCTCACCTGTC TGTCCACCGGAGCCCTCATGACAGGCTATACCGGAGACTTTGACTCCGTGATTGACTGTAACACATGCGTCACCCAAACC GTGGALTTTAGCCTCGACCCTAACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTCGCGGAGGCCAAATCGTCGGCGG AGTGTATCTGCTCCCAGAAGGGGACCCAGAAGGGCTCTGGCTCACGAGGAGTGAGAGTGCTCGAGGATGGCGTCAACTATG CCACAGGCAATCTGCCTGGCTGTAGCTTTAGCATTTTCCTCAGCAAATTCGGATACGGAGCCAAAGACGTCAGGTGTCAC GCTAGGAAAGCCGTCGCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAAACCCCTAGCCAAAACATTCAGCT GCCTCTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCCTGAGAGACTGGCTAGCTGTAGGAGACTGACAGTGGTCCTG ${\tt CGACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCTATCATTCAGAGACTGCATCGCCTCA}$ GCGCTTTCTCCTGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTAC ACAAACGTGGALCAAGACCTCTACAGATTCGTCGCCCCTGGCGAAAGGCCCTAGCGGAATGTTTGACTCCAGCGTCCTGTG TGCCTTGCTCCTTCACAACCCTCCCCGCTCTGTCCACCGGACTGAGAAAGCTCGGCGTCCCCCCTCTGAGAGCCTGGAGG CATAGGGCTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGGCGGAAGGGCTAGCCCTCTGACAACCTCCCAGACACTGCT CTTCAATATCCTCGGCGGATGGGTCGCCGCTCAGCTCGCCGCTCCCGGAGCCGCTACCGCTCTGTGGATtCTCCAGGCTA GCCTCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATGGTGAAAAAAC GGAACCATGAGGATTGTGGGACCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGG AGAGGTCGCCTCAGCACAACCGGAGAGATTCCCTTTTACGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGAC TCCTGGCTCGGCAATATCATTAGGGTCAGCGCTGAGGAATACGTCGAGGATTAGGAGAGTGGGAGACTTTCACTATGTGAC CCCTCCCAGAAAGAAAAGGACAGTGGTCCTGACAGAGTCCACCCTCAGCACAGCCCTCGCCGAACTGGCTACCAAAAGC TTTGGCTCCAGCTCCACCTCCGGCATTACCGGAGACAATACCACAACCTCCGTGTCCTGCCAAAGGGGGATACAAAGGCGT $\tt CTGGAGAGGCGATGGCATTATGCATACCAGATGCCATTGCGGAGCCGAAATCACAGGCCATGTGTTTCTGGTCGGCCAAC$ TGTTTACCTTTAGCCCTAGGAGACACTGGACCACACGGGATGCAATTGCTCCATCTTATCCCGGACACATTTTCGTCGGC GCTGGCCTCGCCGGAGCCGCTATCGGAAGCGTCGGCCTCGGCAAAGTGCTCGTGGATATCCTCGCCGGATACGGAGCCGG AGACATTTGGGATTGGATTTGCGAAGTGCTCAGCGATTTCAAAACCTGGCTGAAAGCCCAAACTGATGCCCCAACTGCCTG GCATTCCCTTTAACTCCAGCATTGTGTATGAGGCTGCCGATGCCATTCTGCATACCCCTGGCTGTGTGTCTTTGCGTCAGG GAAGGCAATGCCTCCAGGTGTAGCTCCGGCTGTCCCGAAAGGCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGG ATGGGGACCCATTAGCTATGCCAATGGCTCCAGGACAGAGGAAGCCATTTACCAATGCTGTGACCTCGACCTCAGGCTA GGGTCGCCATTAAGTCCCTGACAGAGAGACTGTATGTGGGAGTGTCCAAGGGATGGAGACTGCTCGCCCCTATCACAGCC TATGCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCTGACATTCTTTAGCGTCCTGATTGCCAGAGACCA ACTGGAACAGGCTCTGGATTGCGAAATCTATGGCGCTTGCTATAGCATTGAGCCTCTGGATTGCCAAGTGCCTAGCCCTG ATTAAGGCTAGGGCTGCCTGTAGGGCTGCCGGACTGCAAGACTGTACCATGCTGGTCTGCGGAGACGATCTGGTCGTGAT TATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATACGGAAAGTTTC TGGCTGACGGATGCAATTGGACAAGGGGAGAGAGATGCGATCTGGAAGACAGAAGACAGAAGCGAACTGTCCCCCCTCCTG CTCAGCACAACCCAATGGCAAACCGGACACAGAATGGCTTGGGATATGATGATGAATTGGTCCCCCACAGCCGCTCTGGT CATGGCTCAGCTCCTGAGAATCCCTCAGGCTCCCGGAGCCCTCGTGGTCGGCGTCGTCGTCGCCGCTATCCTCAGGAGAC ACGTCGGCCCTGGCGAAGGCGCTGTGCAATGGATGAACAGACACGATAGCCCTGACGCTGAGCTCATCGAAGCCAATCTG CTCTGGAGACAGGAAATGGGAGGCAATATCACAAGGGTCGAGTCCGAGAATGAGGGAGTGTTTACCGGACTGACACACAT TGACGCTCACTTTCTGTCCCAGACAAAGCAAAGCGGAGAGATTTCCCTTACCTCGTGGCTAGGGGAAGGACAGCCTA TCCCTAAGGCTAGGAGACCCGAAGCCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAATCTGATTGTG TTTCCCGATCTGGGAGTGAGAGTGTGTGAGAAAATGGCTCTGTATGACGTCGTGTGCCAAGCTCCCCCTCGCCGTCATGGG ATACGCTACCGGAAACCTCCCCGGATGCTCCTTCTCCATCTTTCTGCCCCCCTGTCCTGCCTCACCGTCCCCGCTA GCGCTTACCAACTGGGAAAGGTCCTGGTTGGALATTCTGGCTGGCTATGGCGTTGGCGTCGCCGGAGCCCTCGTGGCTTTC AAAATCATGAGCGGAGAGGTCAGCTATAGCTCCATGCCTCCCCTCGAGGGAGAGCCTGGCGATCCCGATCTGTCCGACGG **AAGCTGGAGCACAGTGTCCAGCGAAGCCGGAAGGCAAGAGATGGGCGGAAACATTACCAGAGTGGAAAGCGAAAACAAAG** TGGTCATCCTCGACTCCTTCGATCCCTCGTGGCTGAGGAAGTGGGATGGCCTGCCCCTCAGGGAAGCAGAAGCCTCACC CCTTGCACATGCGGAAGCTCCGACCTCTACCTCGTGACAAGGCATGCCGATGGCTGTAGCGGAGGCGCTTACGATATCAT TATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGGCATTGGCACAGTGCTCACCTTTACCATTGAGACAA $\tt CCACACTGCCTCAGGATGCCGTCAGCAGAACCCAAAGGAGGGCAGAACCGGAAGGGGGAAAGCCTGGCATTGACTGTTTC$ AGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTgGACTATCCCCTA TCTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCCGCCTCGTGACACCCTGTGCCGCTTGAGGAACAGA

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AACTGCCTATCAATGCCCTCAGCAATAGCCTCCTGAGACACCATAACCTCGTGTATATCTCCAGCGAATGCACAACCCCT TGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGGATCTGTCAGGTCCTGTCCGACTTTAAGACATGGCTCAAGGCTAA GCTCATGCCTCAGCTCCCCGGAATCCCTTTCGTCAGCTGTCAGGAGAGGGCTATAAGGGGAGTGTGGAGGGGAGACGGAAGCG GACCCTGGATCACCCCAGATGCCTCGTGGATTACCCTTACAGACTGTGGCACTATCCCTGTACCATTAACTATACCATT TTCAAAagatctTGAgtcgacgaattcgcc

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Melanoma Savine design

Two savines - one containing scrambled melanocyte differentiation Ags
- one containing scrambled melanoma cancer specific Ags

Genes in melanocyte differentiation Savine

qp100

MDLVLKRCLLHLAVIGALLAVGATKVPRNQDWLGVSRQLRTKAWNRQLYPEWTEAQRLDCWRGGQVSLKVSNDGPTLI
GANASFSIALNFPGSQKVLPDGQVIWVNNTIINGSQVWGGQPVYPQETDDACIFPDGGPCPSGSWSQKRSFVYVWKTW
GQYWQVLGGPVSGLSIGTGRAMLGTHTMEVTVYHRRGSRSYVPLAHSSSAFTITDQVPFSVSVSQLRALDGGNKHFLR
NQPLTFALQLHDPSGYLARADLSYTWDFGDSSGTLISRALVVTHTYLEPGPVTAQVVLQAAIPLTSCGSSPVPGTTDG
HRPTAEAPNTTAGQVPTTEVVGTTPGQAPTAEPSGTTSVQVPTTEVISTAPVQMPTAESTGMTPEKVPVSEVMGTTLA
EMSTPEATGMTPAEVSIVVLSGTTAAQVTTTEWVETTARELPIPEPEGPDASSIMSTESITGSLGPLLDGTATLRLVK
RQVPLDCVLYRYGSFSVTLDIVQGIESAEILQAVPSGEGDAFELTVSCQGGLPKEACMBISSPGCQPPAQRLCQPVLP
SPACQLVLHQILKGGSGTYCLNVSLADTNSLAVVSTQLIMPGQEAGLGQVPLIVGILLVLMAVVLASLIYRRRLMKQD
FSVPOLPHSSSHWLRLPRIFCSCPIGENSPLLSGOOV

MART

MPREDAHFIYGYPKKGHGHSYTTAEEAAGIGILTVILGVLLLIGCWYCRRRNGYRALMDKSLHVGTQCALTRRCPQEG FDHRDSKVSLQEKNCEPVVPNAPPAYEKLSAEQSPPPYSP

TRP-1

PAFLTWHRYHLLRLEKDMQEMLQEPSFSLPYWNFATGKNVCDICTDDLMGSRSNFDSTLISPNSVFSQWRVVCDSLKD YDTLGTLCNSTEDGPIRRNPAGNVARPMVQRLPEPQDVAQCLEVGLFDTPPFYSNSTNSFRNTVEGYSDPTGKYDPAV RSLHNLAHLFLNGTGGQTHLSSQDPIFVLLHTFTDAVFDEWLRRYNADISTFPLENAPIGHNRQYNMVPFWPPVTNTE MFVTAPDNLGYTYE

Tyros

MLLAVLYCLLWSFQTSAGHFPRACVSSKNLMEKECCPPWSGDRSPCGQLSGRGSCQNILLSNAPLGPQFPFTGVDDRE SWPSVFYNRTCQCSGNFMGFNCGNCKFGFWGPNCTERLLVRRNIFDLSAPEKDKFFAYLTLAKHTISSDYVIPIGTY GQMKNGSTPMFNDINIYDLFVWMHYYVSMDALLGGSEIWRDIDFAHEAPAFLPWHRLFLLRWEQEIQKLTGDENFTIP YWDWRDAEKCDICTDEYMGGQHPTNPNLLSPASFFSSWQIVCSRLEEYNSHQSLCNGTPEGPLRRNPGNHDKSRTPRL PSSADVEFCLSLTQYESGSMDKAANFSFRNTLEGFASPLTGIADASQSSMHNALHIYMNGTMSQVQGSANDPIFLLHH AFVDSIFEQWLQRHRPLQEVYPEANAPIGHNRESYMVPFIPLYRNGDFFISSKDLGYDYSYLQDSDPDSFQDYIKSYL EQASRIWSWLLGAAMVGAVLTALLAGLVSLLCRHKRKQLPEEKOPLLMEKEDYHSLYOSHL

TRP2

MSPLWWGFLLSCLGCKILPGAQGQFPRVCMTVDSLVNKECCPRLGAESANVCGSQQGRQQCTEVRADTRPWSGPYILR NQDDRELWPRKFFHRTCKCTGNFAGYNCGDCKFGWTGPNCERKKPPVIRQNIHSLSPQEREQFLGALDLAKKRVHPDY VITTQHWLGLLGPNGTQPQFANCSVYDFFVWLHYYSVRDTLLGPGRPYRAIDFSHQGPAFVTWHRYHLLCLERDLQRL IGNESFALPYWNFATGRNECDVCTDQLFGAARPDDPTLISRNSRFSSWETVCDSLDDYNHLVTLCNGTYEGLLRRNQM GRNSMKLPTLKDIRDCLSLQKFDNPPFFQNSTFSFRNALEGFDKADGTLDSQVMSLHNLVHSFLNGTNALPHSAANDP IFVVLHSFTDAIFDEWMKRFNPPADAWPQELAPIGHNRMYNMVPFFPPVTNEELFLTSDQLGYSYAIDLPVSVEETPG WPTTLLVVMGTLVALVGLFVLLAFLQYRRLRKGYTPLMETHLSSKRYTEEA

MC1R

MAVQGSQRRLLGSLNSTPTAIPQLGLAANQTGARCLEVSISDGLFLSLGLVSLVENALVVATIAKNRNLHSPMYCFIC CLALSDLLVSGTNVLETAVILLLEAGALVARAAVLQQLDNVIDVITCSSMLSSLCFLGAIAVDRYISIFYALRYHSIV TLPRAPRAVAAIWVASVVFSTLFIAYYDHVAVLLCLVVFFLAMLVLMAVLYVHMLARACQHAQGIARLHKRQRPVHQG FGLKGAVTLTILLGIFFLCWGPFFLHLTLIVLCPEHPTCGCIFKNFNLFLALIICNAIIDPLIYAFHSQBLRRTLKEV LTCSW

MUC1F

 ${\tt MTPGTQSPFFLLLLTVLTVVTGSGHASSTPGGEKETSATQRSSVPSSTEKNAVSMTSSVLSSHSPGSGSSTTQGQDVTLAPATEPASGSAATWGQDVTSVPVTRPALGSTTPPAHDVTSAPDNK$

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MUC1R

NRPALGSTAPPVHNVTSASGSASGSASTLVHNGTSARATTTPASKSTPFSIPSHHSDTPTTLASHSTKTDASSTHHSS VPPLTSSNHSTSPQLSTGVSFFFLSFHISNLQFNSSLEDPSTDYYQELQRDISEMFLQIYKQGGFLGLSNIKFRPGSV VVQLTLAFREGTINVHDVETQFNQYKTEAASRYNLTISDVSVSDVPFPFSAQSGAGVPGWGIALLVLVCVLVALAIVY LIALAVCQCRRKNYGQLDIFPARDTYHPMSEYPTYHTHGRYVPPSSTDRSPYEKVSAGNGGSSLSYTNPAVAAASANL

NB Muc 1 Repeat sequences in the middle of the gene were removed

Genes in melanoma specific Savine

BAGE

MAARAVFLALSAQLLQARLMKEESPVVSWRLEPEDGTALCFIF

GAGR-1

 ${\tt MSWRGRSTYRPRPRRYVEPPEMIGPMRPEQFSDEVEPATPEEGEPATQRQDPAAAQEGEDEGASAGQGPKPEADSQEQGEPQTGCECEDGPDGQEMDPPNPEEVKTPEEEMRSHYVAQTGILWLLMNNCFLNLSPRKP$

gp100In4

SWSQKRSFVYVWKTWGEGLPSQPIIHTCVYFFLPDHLSFGRPFHLNFCDFL

MAGE-1

MSLEQRSLHCKPEEALEAQQEALGLVCVQAATSSSSPLVLGTLEEVPTAGSTDPPQSPQGASAFPTTINFTRQRQPSE GSSSREEEGPSTSCILESLFRAVITKKVADLVGFLLLKYRAREPVTKAEMLESVIKNYKHCPPEIFGKASESLQLVFG IDVKEADPTGHSYVLVTCLGLSYDGLLGDNQIMPKTGFLIIVLVMIAMEGGHAPEEEIWEELSVMEVYDGREHSAYGE PRKLLTQDLVQEKYLEYRQVPDSDPARYEFLWGPRALAETSYVKVLEYVIKVSARVRFFFPSLREAALREEEEGV

MAGE-3

MPLEQRSQHCKPEEGLEARGEALGLVGAQAPATEEQEAASSSSTLVEVTLGEVPAAESPDPPQSPQGASSLPTTMNYP LWSQSYEDSSNQEEEGPSTFPDLESEFQAALSRKVAELVHFLLLKYRAREPVTKAEMLGSVVGNWQYFPPVIFSKASS SLQLVFGIELMEVDPIGHLYIFATCLGLSYDGLLGDNQIMPKAGLLIIVLAIIAREGDCAPEEKIWEELSVLEVFEGR EDSILGDPKKLLTQHFVQENYLEYRQVPGSDPACYEFLWGPRALVETSYVKVLHHMVKISGGPHISYPPLHEWVLREG EE

PRAME

MERRRLWGSIQSRYISMSVWTSPRRLVELAGQSLLKDEALAIAALELLPRELFPPLFMAAFDGRHSQTLKAMVQAWPF
TCLPLGVLMKGQHLHLETFKAVLDGLDVLLAQEVRPRRWKLQVLDLRKNSHQDFWTVWSGNRASLYSFPEPEAAQPMT
KKRKVDGLSTEAEQPFIPVEVLVDLFLKEGACDELFSYLIEKVKRKKNVLRLCCKKLKIFAMPMQDIKMILKMVQLDS
IEDLEVTCTWKLPTLAKFSPYLGQMINLRRLLLSHIHASSYISPEKEEQYIAQFTSQFLSLQCLQALYVDSLFFLRGR
LDQLLRHVMNPLETLSITNCRLSEGDVMHLSQSPSVSQLSVLSLSGVMLTDVSPEPLQALLERASATLQDLVFDECGI
TDDQLLALLPSLSHCSQLTTLSFYGNSISISALQSLLQHLIGLSNLTHVLYPVPLBSYEDIHGTLHLERLAYLHARLR
ELLCELGRPSMVWLSANPCPHCGDRTFYDPEPILCPCFMPN

TRP2IN2

LMETHLSSKRYTEEAGGFFPWLKVYYYRFVIGLRVWQWEVISCKLIKRATTRQP

NYNSO1a

 ${\tt MQAEGRGTGGSTGDADGPGGPGIPDGPGGNAGGPGEAGATGGRGPRGAGAARASGPGGGAPRGPHGGAASGLNGCCRC}\\ {\tt GARGPESRLLEFYLAMPFATPMEAELARRSLAQDAPPLPVPGVLLKEFTVSGNILTIRLTAADHRQLQLSISSCLQQLSLLMWITQCFLPVFLAQPPSGQRR}\\$

NYNSO1b

MLMAQEALAFLMAQGAMLAAQERRVPRAAEVPGAQGQQGPRGREEAPRGVRMAARLOG

LAGE1

Differentiation Savine Scramble process

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MQAEGQGTGGSTGDADGPGGPGIPDGPGGNAGGPGEAGATGGRGPRGAGAARASGPRGGAPRGPHGGAASAQDGRCPC GARRPDSRLLQLHITMPFSSPMEABLVRRILSRDAAPLPRPGAVLKDFTVSGNLLFIRLTAADHRQLQLSISSCLQQL SLLMWITQCFLPVFLAQAPSGQRR

```
Disease name
                : melanoma
 Input filename
               : Diffmucg.txt
 Output filename : Diffmucs.txt
 Number genes
                : 8
 Number segments : 187
Segment length : 30
Segment overlap : 15
 Segments in original order:
         : gp100
Segment# : 1
Offset
         : 1
1st Codon : 1
 A A M D L V L K R C L L H L A V I G A L L A V G A T K V P R
GCCGCTATGGATCTGGTCCTGAAAAGGTGTCTCCACCTCGCCGTCATCGGAGCCCTCCTGGCTGTGGGAGCCACAAAGGTCCCCAGA
         : gp100
Segment#
        : 2
Offset
         : 16
1st Codon : 1
 V I G A L L A V G 'A T K V P R N Q D W L G V S R Q L R T K A
GTGATTGGCGCTCTGCTCGCCGTCGGCGCTACCAAAGTGCCTAGGAATCAGGATTGGCTCGGCGTCAGCAGACAGCTCAGGACAAAGGCT
Gene
         : gp100
Segment# : 3
Offset
         : 31
1st Codon : 1
 N Q D W L G V S R Q L R T K A W N R Q L Y P E W T E A Q R L
AACCAAGACTGGCTGGGAGTGTCCAGGCAACTGAGAACCAAAGCCTGGAACAGCTCTACCCTGAGTGGACCGAAGCCCAAAGGCTC
         : gp100
Gene
Segment# : 4
         : 46
Offset
1st Codon : 1
W N R Q L Y P B W T B A Q R L D C W R G G Q V S L K V S N D
TGGAATAGGCAACTGTATCCCGAATGGACAGAGGCTCAGAGACTGGATTGCTGGAGGGGGGGCCAAGTGTCCCTGAAAGTGTCCCAACGAT
         : gp100
Segment# : 5
Offset
        : 61
1st Codon : 1
D C W R G G Q V S L K V S N D G P T L I G A N A S F S I A L
GACTGTTGGAGAGGCGGACAGGTCAGCCTCAAGGTCAGCAATGACGGACCCACACTGATTGGCGCTAACGCTTAGCATTGCCCTC
Gene
         : gp100
Segment#
        : 6
         : 76
1st Codon : 1
G P T L I G A N A S F S I A L N F P G S Q K V L P D G Q V I
GGCCCTACCCTCATCGGAGCCAATGCCTCCTTCTCCATCGCTCTGAATTTCCCTGGCTCCCAGAAAGTGCTCCCCGATGGCCAAGTGATT
Gene
        : gp100
Segment# : 7
Offset
        : 91
1st Codon : 1
N F P G S Q K V L P D G Q V I W V N N T I I N G S Q V W G G
AACTTTCCCGGAAGCCAAAAGGTCCTGCCTGACGGACAGGTCATCTGGGTGAATAACACAATCATTAACGGAAGCCAAGTGTGGGGCGGA
        : qp100
Segment# : 8
Offset
        : 106
1st Codon : 1
```

Figure 27 (Cont)

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W V N N T I I N G S Q V W G G Q P V Y P Q B T D D A C I F P
 TGGGTCAACAATACCATTATCAATGGCTCCCAGGTCTGGGGAGGCCAACCCGTCTACCCTCAGGAAACCGATGACGCTTGCATTTTCCCT
         : qp100
  Segment# : 9
  Offset
         : 121
 1st Codon : 1
  Q P V Y P Q B T D D A C I P P D G G P C P S G S W S Q K R S
 CAGCCTGTGTATCCCCAAGAGACGATGCCTGTATCTTTCCCGATGGCGGACCCTGTCCCTCCGGCTCCTGGTCCCAGAAAAGGTCC
         : qp100
 Segment# : 10
 Offset
         : 136
 1st Codon : 1
  D G G P C P S G S W S Q K R S F V Y V W K T W G Q Y W Q V L
 GACGGAGGCCCTTGCCCTAGCGGAAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGACAGTATTGGCAAGTGCTC
         : qp100
 Segment# : 11
Offset : 151
 Offset
        : 151
 1st Codon: 1
PVYVWKTWGQYWQVLGGPVSGLSIGTGRAM
 TTCGTCTACGTCTGGAAAACCTGGGGCCAATACTGGCAGGTCCTGGGAGGCCTGTGTCCGGCCTCAGCATTGGCACAGGCAGAGCCATG
         : gp100
 Segment# : 12
 Offset
        : 166
 1st Codon : 1
 G G P V S G L S I G T G R A M L G T H T M E V T V Y H R R G
 Gene
         : gp100
 Segment# : 13
 Offset
        : 181
 1st Codon : 1
 LGTHTMEVTVYHRRGSRSYVPLAHSSSAFT
 CTGGGAACCCATACCATGGAGGTCACCGTCTACCATAGGAGAGGCTCCAGGGTCCTACGTCCCCCTCGCCCATAGCTCCAGCGCTTTCACA
Gene : gp100
Segment# : 14
Offset
        : 196
1st Codon : 1
 S R S Y V P L A H S S S A F T I T D Q V P P S V S V S Q L R
AGCAGAAGCTATGTGCCTCTGGCTCACCTCCAGCTCCGCCTTTACCATTACCGATCAGGTCCCCTTTAGCGTCAGCGTCAGCCAACTGAGA
Gene
        : qp100
Segment# : 15
Offset
        : 211
1st Codon : 1
 I T D Q V P F S V S V S Q L R A L D G G N K H F L R N Q P L
ATCACAGACCAAGTGCCTTTCTCCGTGTCCGTGTCCCAGCTCAGGGCTCTGGATGGCGGAAACAACCACTTTCTGAGAAACCACCCCTC
Gene
        : gp100
Segment# : 16
Offset
        : 226
1st Codon : 1
 A L D G G N K H F L R N Q P L T F A L Q L H D P S G Y L A E
GCCCTCGACGGAGGCAATAAGCATTTCCTCAGGAATCAGCCTCTGACATTCGCTCTGCAACTGCATGACCCTAGCGGATACCTCGCCGAA
Gene
        : gp100
Segment# : 17
Offset
       : 241
1st Codon : 1
 T F A L Q L H D P S G Y L A E A D L S Y T N D F G D S S G T
ACCITTGCCCTCCAGCTCCACGATCCCTCCGGCTATCTGGCTGAGGCTGACCTCAGCTATACCTGGGACTTTGGCGATAGCTCCGGCACA
       : gp100
Gene
Segment# : 18
Offset
       : 256
1st Codon : 1
 A D L S Y T W D F G D S S G T L I S R A L V V T H T Y L E P
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Gene : qp100 Segment# : 19 Offset : 271 1st Codon : 1 L I S R A L V V T H T Y L B P G P V T A Q V V L Q A A Y P L CTGATTAGCAGAGCCCTCGTGGTCACCCATACCTATCTGGAACCCGGACCCGTCACCGCTCAGGTCGTGCTCCAGGCTGCCATTCCCCTC Gene : gp100 Segment# : 20 Offset : 286 1st Codon : 1 G P V T A Q V V L Q A A I P L T S C G S S P V P G T T D G H GGCCCTGTGACAGCCCAAGTGGTCCTGCAAGCCGCTATCCCTCTGACAAGCTGTGGCTCCAGCCCTGTGCCTGGCACAACCGATGGCCAT Gene : gp100 Segment# : 21 Offset : 301 1st Codon : 1 T S C G S S P V P G T T D G H R P T A B A P N T T A G Q V P Gene : qp100 Segment# : 22 : 316~ Offset 1st Codon : 1 RPTAEAPNTTAGQVPTTEVVGTTPGQAPTA AGGCCTACCGCTGAGGCTCCCAATACCACAGCCGGACAGGTCCCCACAACCGAAGTGGTCGGCACAACCCCTGGCCAAGCCCCTACCGCT : gp100 : 23 Segment# Offset : 331 1st Codon : 1 TTEVVGTTPGQAPTAEPSGTTSVQVPTTEV ACCACAGAGGTCGTGGGAACCACACCCGGACAGGCTCCCACAGCCGGAACCCTCCGGCACAACCTCCGTGCAAGTGCCTACCACAGAGGTC Gene : gp100 Segment# : 24 Offset : 346 B P S G T T S V Q V P T T E V I S T A P V Q M P T A E S T G GAGCCTAGCGGAACCACAAGCGTCCCAGGTCCCCACAACCGAAGTGATTAGCACAGCCCCTGTGCAAATGCCTACCGCTGAGTCCACCGGA Gene : gp100 Segment# : 25 Offset : 361 1st Codon : 1 I S T A P V Q M P T A E S T G M T P E K V P V S E V M G T T ATCTCCACCGCTCCCGTCCAGATGCCCACAGCCGAAAGCACAGGCATGACCCCTGAGAAAGTGCCTGTGTCCGAGGTCATGGGAACCACA Gene : gp100 Segment# : 26 Offset : 376 M T P E K V P V S E V M G T T L A E M S T P E A T G M T P A ATGACACCCGAAAAGGTCCCCGTCAGCGAAGTGATGGGCACAACCCTCGCCGAAATGTCCACCCCTGAGGCTACCGGAATGACACCCGGCT Gene : gp100 Segment# : 27 Offset : 391 1st Codon : 1 LABMSTPEATGMTPAEVSIVVLSGTTAAQV CTGGCTGAGATGAGCACACCCGAAGCCACAGGCATGACCCCTGCCGAAGTGTCCATCGTCGTCGTGCTCAGCGGAACCACAGCCGCTCAGGTC Gene : gp100 Segment# : 28 Offset : 406 1st Codon : 1 BVSIVVLSGTTAAQVTTTBWVETTARELPI Gene : gp100

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Segment# : 29 Offset : 421 1st Codon : 1 T T T B W V B T T A R B L P I P B P B G P D A S S I M S T B ACCACAACCGAATGGTCGAGACAACCGCTAGGGAACTGCCTATCCCTGAGCCTGAGGGACCCGATGCTTCCAGCATTATGTCCACCGAA Gene : gp100 Segment# : 30 Offset : 436 1st Codon : 1 P B P B G P D A S S I M S T E S I T G S L G P L L D G T A T CCCGAACCCGAAGGCCCTGACGCTAGCTCCATCATGAGCACAGAGTCCATCACAGGCTCCCTGGGACCCCTCCTGGATGGCACAGCCACA Gene : gp100 Segment# : 31 Offset : 451 1st Codon : 1 SITGSLGPLLDGTATLRLVKRQVPLDCVLY AGCATTACCGGAAGCCTCGGCCCTCTGCTCGACGGAACCGCTACCCTCAGGCTCGTGAAAAGGCAAGTGCCTCTGGATTGCGTCCTGTAT Gene : gp100 Segment# : 32 Offset : 466 1st Codon : 1 LRLVKRQVPLDCVLYRYGSFSVTLDIVQGI CTGAGACTGGTCAAGAGACAGGTCCCCCTCGACTGTGGCTCTACAGATACGGAAGCTTTAGCGTCACCCTCCACATTGTGCAAGGCATT Gene : gp100 Segment# : 33 Offset : 481 1st Codon : 1 RYGSPSVTLDIVQGIBSARILQAVPSGEGD AGGTATGGCTCCTTCTCCGTGACACTGGATATCGTCCAGGGAATCGAAAGCGCTGAGATTCTGCAAGCCGTCCCCTCCGGCGAAGGCGGAT : qp100 Segment# : 34 Offset : 496 1st Codon: 1
ESAEILQAVPSGEGDAFELTVSCQGGLPKE CAGTCCGCCGAAATCCTCCAGGCTGTGCCTAGCGGAGAGGGAGACGCTTTCGAACTGACAGTGTCCTGCCAAGGCGGACTGCCTAAGGAA Gene : gp100 Segment# : 35 1st Codon : 1 A F B L T V S C Q G G L P K B A C M B I S S P G C Q P P A Q GCCTTTGAGCTCACCGTCAGCTGTCAGGGAGGCCTCCCCAAAGAGGCTTGCATGGAGATTAGCTCCCCGGATGCCAACCCCCTGCCCAA Gene : gp100 Segment# : 36 : 526 Offset A C M E I S S P G C Q P P A Q R L C Q P V L P S P A C O L V : gp100 Gene Segment# : 37 Offset : 541 1st Codon : 1 R L C Q P V L P S P A C Q L V L H Q I L K G G S G T Y C L N AGGCTCTGCCAACCCGTCCTGCCTAGCCCTGCCTGTCAGCCCGGCTCCACCAAATCCTCAAGGGAGGCTCCGGCACATACTGTCTGAAT Gene : gp100 Segment# : 38 Offset : 556 1st Codon : 1 L H Q I L K G G S G T Y C L N V S L A D T N S L A V V S T O CTGCATCAGATTCTGAAAGGCGGAAGCGGAACCTATTGCCTCAACGTCAGCCTCGCCGATACCAATAGCCTCGCCGTCGTCTCCACCCAA : gp100 Gene Segment# : 39 Offset : 571

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1st Codon : 1
 V S L A D T N S L A V V S T Q L I M P G Q E A G L G Q V P L
 GTGTCCCTGGCTGACACAAACTCCCTGGCTGTGGTCAGCACACACCTCATCATGCCCGGACAGGAAGCCGGACTGGGACAGGTCCCCCTC
 Gene
         : gp100
 Segment# : 40
 Offset
        : 586
 1st Codon : 1
 LIMPGQBAGLGQVPLIVGILLVLMAVVLAS
 CTGATTATGCCTGGCCAAGAGGCTGGCCTCGGCCAAGTGCCTCTGATTGTGGGAATCCTCCTGGTCCTGATGGCCGTCGTGCTCGCCTCC
Cene
Segment#
        : 41
        : 601
Offset
1st Codon : 1
 I V G I L L V L M A V V L A S L I Y R R R L M K Q D P S V P
ATCGTCGGCATTCTGCTCGTCGTCGTGGTCCTGGCTAGCCTCATCTATAGGAGAAGGCTCATGAAACAGGATTTCTCCGTGCCT
Gene
         : gp100
Segment# : 42
Offset
        : 616
1st Codon : 1
 LIYRRRLMKQDPSVPQLPHSSSHWLRLPRI
CTGATTTACAGAAGGAGACTGATGAAGCAAGACTTTAGCGTCCCCCAACTGCCTCACTCCAGCTCCCACTGGCTGAGACTGCCTAGGATT
Gene
        : gp100
Segment# : 43
Offset
        : 631
1st Codon : 1
 Q L P H S S S H W L R L P R I F C S C P I G B N S P L L S G
CAGCTCCCCCATAGCTCCAGCCATTGGCTCAGGCTCCCCAGAATCTTTTGCTCCTGCCCTATCGGAGAGAATAGCCCTCTGCTCAGCGGA
Gene
        : gp100
Segment# : 44
Offset
       : 646
1st Codon : 1
PCSCPIGENSPLLSGQQVAA
TTCTGTAGCTGTCCCATTGGCGAAAACTCCCCCCTCCTGTCCGGCCAACAGGTCGCCGCT
        : MART
Segment# : 1
Offset
        : 1
1st Codon : 1
A A M P R E D A H P I Y G Y P K K G H G H S Y T T A B E A A
GCCGCTATGCCTAGGGAAGACGCTCACTTTATCTATGGCTATCCCAAAAAGGGACACGGACACTCCTACACAACCGCTGAGGAAGCCGCT
Gene
        : MART
Segment# : 2
Offset
1st Codon : 1
K K G H G H S Y T T A B B A A G I G I L T V I L G V L L L I
AAGAAAGGCCATGGCCATAGCTATACCACAGCCGAAGAGGCTGCCGGAATCGGAATCCTCACCGTCATCCTCGGCGTCCTGCTCCTGATT
Gene
        : MART
Segment# : 3
Offset
       : 31
1st Codon : 1
G I G I L T V I L G V L L L I G C W Y C R R R N G Y R A L M
GGCATTGGCATTCTGACAGTGATTCTGGGAGTGCTCCTGCTCATCGGATGCTGGTACTGTAGGGAAATGGCTATAGGGCTCTGATG
        : MART
Gene
Segment# : 4
Offset
       : 46
G C W Y C R R R R G Y R A L M D K S L H V G T Q C A L T R R
GGCTGTTGGTATTGCAGAAGGAGAACGGATACAGAGCCCTCATGGATAAGTCCCTGCATGTGGGAACCCAATGCGCTCTGACAAGGAGA
Gene
        : MART
Segment# : 5
Offset
       : 61
1st Codon : 1
D K S L H V G T Q C A L T R R C P Q E G F D H R D S K V S L
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GACAAAAGCCTCCACGTCGCCACACAGTGTGCCCTCACCAGAAGGTGTCCCCAAGAGGGGATTCGATCACAGAGACTCCAAGGTCAGCCTC
        : MART
 Gene
 Segment# : 6
 Offset
        : 76
 1st Codon : 1
 C P Q B G F D H R D S K V S L Q B K N C B P V V P N A P P A
 TGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAGTGTCCCTGCAAGAGAAAAACTGTGAGCCTGTGGTCCCCAATGCCCCTCCCGCT
        : MART
 Gene
 Segment# : 7
 Offset
        : 91
1st Codon : 1
 Q B K N C B P V V P N A P P A Y B K L S A B Q S P F P Y S P
Gene
Segment# : 8
Offset
       : 106
1st Codon : 1
 YEKLSABQSPPPYSPAA
TACGAAAAGCTCAGCGCTGAGCAAAGCCCTCCCCCTTACTCCCCCGCTGCC
Gene
        : TRP-1
Segment# : 1
Offset
       : 1
1st Codon : 1
 A A P A F L T W H R Y H L L R L B K D M Q B M L Q E P S, F S
GCCGCTCCCGCTTTCCTCACCTGGCACAGATACCATCTGCTCAGGCTCGAGAAAGACATGCAGGAAATGCTCCAGGAACCCTCCTTCTCC
Gene
        : TRP-1
Segment# : 2
Offset
       : 16
1st Codon : 1
 L B K D M Q B M L Q B P S F S L P Y W N F A T G K N V C D I
Gene
        : TRP-1
Segment# : 3
Offset
       : 31
1st Codon : 1
 L P Y W N F A T G K N V C D I C T D D L M G S R S N F D S T
CTGCCTTACTGGAACTTTGCCACAGGCAAAAACGTCTGCGATATCTGTACCGATGACCTCATGGGAAGCAGAAGCAATTTCGATAGCACA
Segment# : 4
Offset
       : 46
1st Codon : 1
C T D D L M G S R S N. P D S T L I S P N S V F S Q W R V V C
TGCACAGACGATCTGATGGGCTCCAGGTCCAACTTTGACTCCACCCTCATCTCCCCCAATAGCGTCTTCTCCCCAGTGGAGGGTCGTGTT
       : TRP-1
Gene
Segment# : 5
Offset
       : 61
1st Codon : 1
LISPNSVFSQWRVVCDSLEDYDTLGTLCNS
CTGATTAGCCCTAACTCCGTGTTTAGCCAATGGAGAGTGGTCTGCGATAGCCTCGAGGATTACCGTCGGCACACTGTGTAACTCC
       : TRP-1
Gene
Segment# : 6
Offset
      : 76
1st Codon : 1
D S L B D Y D T L G T L C N S T B D G P I R R N P A G N V A
GACTCCCTGGAAGACTATGACACACTGGGAACCCTCTGCAATAGCACAGAGGATGGCCCTATCAGAAGGAATCCCGCTGGCAATGTGGCT
Gene
       : TRP-1
Segment#
      : 7
1st Codon : 1
T B D G P I R R N P A G N V A R P M V Q R L P E P Q D V A Q
ACCGAAGACGGACCCATTAGGAGAAACCCTGCCGGAAACGTCGCCAGACCCCATGGTGCAAAGGCTCCCCGAACCCCCAAGACGTCGCCCAA
```

157/216 Gene : TRP-1 Segment# : 8 Offset : 106 1st Codon : 1 R P M V Q R L P B P Q D V A Q C L B V G L P D T P P P Y S N AGGCCTATGGTCCAGAGACTGCCTGAGGCTCAGGATGTGGCTCAGTGTCTGGAAGTGGGACTGTTTGACACACCCCCTTTCTATAGCAAT : TRP-1 Segment# : 9 Offset : 121 1st Codon : 1 C L E V G L F D T P P F Y S N S T N S F R N T V E G Y S D P ${\tt TGCCTCGAGGCTCTTTGATACCCCTCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCTTTTACTCCAACTCAACTCCAACTCCAACTCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCAACTCCAACTCA$: TRP-1 Segment# : 10 Offset : 136 STN SPR N T V B G Y S D P T G K Y D P A V R S L H N L A AGCACAAACTCCTTCAGAAACACAGTGGAAGGCTATAGCGATCCCACAGGCAAATACGATCCCGCTGTGAGAAGCCTCCACAATCTGGCT : TRP-1 Segment# : 11 Offset : 151 1st Codon : 1 T G K Y D P A V R S L H N L A H L P L N G T G G Q T H L S S Gene : TRP-1 Segment# : 12 Offset : 166 1st Codon : 1 H L F L N G T G G Q T H L S S Q D P I F V L L H T F T D A V CACCTCTTCCTCAACGGAACCGGAGGCCAAACCCATCTGTCCAGCCAAGACCCTATCTTTGTGCTCCTGCATACCTTTACCGATGCCGTC : TRP-1 Gene Segment# : 13 Offset : 181 1st Codon : 1 Q D P I P V L L H T F T D A V F D E W L R R Y N A D I S T P CAGGATCCCATTTTCGTCCTGCTCCACACATTCACAGACGCTGTGTTTGACGAATGGCTCAGGAGATACAATGCCGATATCTCCACCTTT : TRP-1 Segment# : 14 Offset : 196 1st Codon: 1 PDEWLRRYNADISTPPLBNAPIGHNRQYNM : TRP-1 Gene Segment# : 15 : 211 P L R N A P I G H N R Q Y N M V P F W P P V T N T E M F V T CCCTCGAGAATGCCCCTATCGGACACAATAGGCAATACGATATGGTCCCCTTTTGGCCTCCCGTCACCAATACCGAAATGTTTGTGACA : TRP-1 Gene Segment# : 16 Offset : 226 1st Codon : 1 V P F W P P V T N T E M F V T A P D N L G Y T Y E A A GTGCCTTTCTGGCCCCCTGTGACAACACAGAGATGTTCGTCACCGCTCCCGGATAACCTCGGCTATACCTATGAGGCTGCC Gene : Tyros Segment# : 1 Offset A A M L L A V L Y C L L W S F Q T S A G H F P R A C V S S K

Gene : Tyros Segment# : 2

GCCGCTATGCTCCTGGCTGTGCTCTACTGTCTGGTCCTTCCAAACCTCCGCCGGACACTTTCCCAGAGCCTGTGTGTCCCAGCAAA

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Offset
        : 16
 1st Codon : 1
 Q T S A G H P P R A C V S S K N L M B K E C C P P W S G D R
 Gene
        : Tyros
 Segment# : 3
 Offset
        : 31
1st Codon : 1
 N L M B K B C C P P W S G D R S P C G Q L S G R G S C Q N I
AACCTCATGGAAAAGGAATGCTGTCCCCCTTGGTCCGGCGATAGGTCCCCCTGTGGCCAAACTGTCCGGCAGAGGCTCCTGCCAAAACATT
Gene
        : Tyros
Segment# : 4
Offset
       : 46
1st Codon : 1
 SPCGQLSGRGSCQNILLSNAPLGPQPPFTG
AGCCCTTGCGGACAGCTCAGCGGAAGGGGAAGCTGTCAGAATATCCTCCTGTCCAACGCTCCCTCGGCCCTCAGTTTCCCTTTACCGGA
Gene
Segment# : 5
Offset
1st Codon : 1
 L L S N A P L G P Q F P F T G V D D R B S W P S V F Y N R T
CTGCTCAGCAATGCCCCTCTGGGACCCCAATTCCCTTTCACAGGCGTCGACGATAGGGAAAGCTGGCCCTCCGTGTTTTACAATAGGACA
Gene
        : Tyros
Segment# : 6
       : 76
Offset
1st Codon : 1
 V D D R B S W P S V F Y N R T C Q C S G N F M G F N C G N C
GTGGATGACAGAGAGTCCTGGCCTAGCGTCTTCTATAACAGAACCTGTCAGTGTAGCGGAAACTTTATGGGATTCAATTGCGGAAACTGT
Gene
       : Tyros
Segment# : 7
Offset
       : 91
1st Codon : 1
 C Q C S G N F M G F N C G N C K F G F W G P N C T E R R L L
TGCCAATGCTCCGGCAATTTCATGGGCTTTAACTGTGGCAATTGCAAATTCGGATTCTGGGCCCTAACTGTACCGAAAGGAGACTGCTC
       : Tyros
Segment# : 8
       : 106
Offset
1st Codon : 1
K F G F W G P N C T B R R L L V R R N I F D L S A P B K D K
AAGTTTGGCTTTTGGGGACCCAATTGCACAGAGAGAGGCCTCCTGGTCAGGAGAAACATTTTCGATCTGTCCGCCCCTGAGAAACACAAA
Gene
       : Tyros
Segment# : 9
       : 121
Offset
V R R N I F D L S A P E K D K F F A Y L T L A K H T I S S D
Gene
       : Tyros
Segment# : 10
Offset
      : 136
FFAYLTLAKHTISSDYVIPIGTYGQMKNGS
TTCTTTGCCTATCTGACACTGGCTAAGCATACCATTAGCTCCGACTATGTGATTCCCATTGGCACATACGGACAGATGAAGAATGGCTCC
Gene
      : Tyros
Segment# : 11
Offset
      : 151
1st Codon : 1
Y V I P I G T Y G Q M K N G S T P M P N D I N I Y D L P V W
TACGTCATCCCTATCGGAACCTATGGCCAAATGAAAAACCGGAAGCACCCCATGTTCAATGACATTAACATTTACGATCTGTTTGTGTGG
Gene
       : Tyros
Segment# : 12
Offset
      : 166
1st Codon : 1
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T P M F N D I N I Y D L F V W M H Y Y V S M D A L L G G S E
 ACCCCTATGTTTAACGATATCAATATCTATGACCTCTTCGTCTGGATGCACTATTACGTCAGCATGGACGCTCTGCTCGGCGGAAGCGAA
         : Tyros
 Segment# : 13
 Offset
         : 181
 1st Codon : 1
 M H Y Y V S M D A L L G G S E I W R D I D P A H E A P A F L
 ATGCATTACTATGTGTCCATGGATGCCCTCCTGGGAGGCTCCGAGATTTGGAGAGACATTGACTTTGCCCATGAGGCTCCCGCTTTCCTC
         : Tyros
 Gene
 Segment# : 14
 Offset
         : 196
 1st Codon : 1
 I W R D I D F A H E A P A F L P W H R L F L L R W E Q E I Q
 ATCTGGAGGGATATCGATTTCGCTCACGAAGCCCCTGCCTTTCTGCCTTGGCATAGGCTCTTCCTCCTGAGATGGGAACAGGAAATCCAA
 Gene
         : Tyros
 Segment# : 15
 Offset
        : 211
 1st Codon : 1
 PWHRLFLRWEQEIQKLTGDENFTIPYWDW
 CCCTGGCACAGACTGTTTCTGCTCAGGTGGGAGCAAGAGATTCAGAAACTGACAGGCGATGAGAATTTCACAAATCCCTTACTGGGACTGG
         : Tyros
 Segment#
        : 16
Offset
        : 226
1st Codon : 1
 K L T G D B N F T I P Y W D W R D A B K C D I C T D B Y M G
AAGCTCACCGGAGACGAAAACTTTACCATTCCCTATTGGGATTGGAGAGACGCTGAGAAATGCGATATCTGTACCGATGAGTATATGGGA
Gene
         : Tyros
Segment# : 17
Offset
        : 241
1st Codon : 1
 RDAEKCDICTDEYMGGQHPTNPNLLSPASF
AGGGATGCCGAAAAGTGTGACATTTGCACAGACGAATACATGGGCGGACAGCATCCCACAAACCCTAACCTCCTGTCCCCCGCTAGCTTT
Gene
        : Tyros
Segment# : 18
Offset
        : 256
1st Codon : 1
 G Q H P T N P N L L S P A S P F S S W Q I V C S R L B B Y N
GGCCAACACCCTACCAATCCCAATCTGCTCAGCCCTGCCTCCTTCTTTAGCTCCTGGCAAATCGTCTGCTCCAGGCTCGAGGAATACAAT
Gene
        : Tyros
Segment# : 19
Offset
        : 271
1st Codon : 1
 FSSWQIVCSRLBEYNSHQSLCNGTPBGPLR
TTCTCCAGCTGGCAGATTGTGTGTAGCAGACTGGAAGAGTATAACTCCCACCAAAGCCTCTGCAATGGCACACCCGAAGGCCCTCTGAGA
Gene
        : Tyros
Segment# : 20
Offset
        : 286
1st Codon : 1
 S H Q S L C N G T P E G P L R R N P G N H D K S R T P R L P
AGCCATCAGTCCCTGTGTAACGGAACCCCTGAGGGACCCCTCAGGGGAAAACCCTGGCAATCACGATAAGTCCAGGACACCCAGACTGCCT
Gene
        : Tyros
Segment# : 21
Offset
        : 301
1st Codon : 1
R N P G N H D K S R T P R L P S S A D V R F C L S L T Q Y E.
AGGAATCCCGGAAACCATGACAAAAGCAGAACCCCTAGGCTCCCCTCCAGCGCTGACGTCGAGTTTTGCCTCAGCCTCACCCAATACGAA
Gene
        : Tyros
Segment# : 22
Offset
        : 316
1st Codon : 1
S S A D V E F C L S L T Q Y E S G S M D K A A N F S F R N T
AGCTCCGCCGA TGTGGAATTCTGTCTGTCCCTGACACAGTATGAGTCCGGCTCCATGGATAAGGCTGCCAATTTCTCCTTCAGAAACACA
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: Tyros
 Segment# : 23
 Offset
         : 331
 1st Codon : 1
  S G S M D K A A N F S F R N T L E G F A S P L T G I A D A S
 AGCGGAAGCATGGACAAAGCCGCTAACTTTAGCTTTAGGAATACCCTCGAGGGATTCGCTAGCCCTCTGACAGGCATTGCCGATGCCTCC
 Gene
         : Tyros
 Segment# : 24
 Offset
        : 346
 1st Codon : 1
 L B G F A S P L T G I A D A S Q S S M H N A L H I Y M N G T
 CTGGAAGGCTTTGCCTCCCCCTCACCGGAATCGCTGACGCTAGCCAAGCTCCATGCATAACGCTCTGCATATCTATATGAATGGCACA
 Gene
         : Tyros
 Segment# : 25
 Offset
        : 361
 1st Codon : 1
 Q S S M H N A L H I Y M N G T M S Q V Q G S A N D P I F L L
 CAGTCCAGCATGCACAATGCCCTCCACATTTACATGAACGGAACCATGAGCCAAGGCTCCGCCAATGACCCTATCTTTCTGCTC
 Gene
         : Tyros
 Segment# : 26
 Offset
        : 376
1st Codon : 1
 M S Q V Q G S A N D P I F L L H H A F V D S I F E Q W L Q R
ATGTCCCAGGTCCAGGGAAGCGCTAACGATCCCATTTTCCTCCTGCATCACGCTTTCGTCGACTCCATCTTTGAGCAATGGCTCCAGAGA
Gene
         : Tyros
Segment# : 27
Offset
        : 391
 H H A F V D S I P B Q W L Q R H R P L Q B V Y P B A N A P I
{\tt CACCATGCCTTTGTGGATAGCATTTTCGAACAGTGGCTGCAAAGGCATAGGCCTCTGCAAGAGGTCTACCCTGAGGCTAACGCTCCCATT}
Gene
        : Tyros
Segment# : 28
Offset
        : 406
1st Codon : 1
 H R P L Q E V Y P E A N A P I G H N R E S Y M V P F I P L Y
CACAGACCCCTCCAGGAAGTGTATCCCGAAGCCAATGCCCCTATCGGACACAATAGGGAAAGCTATATGGTCCCCTTTATCCCTCTGTAT
        : Tyros
Gene
Segment# : 29
Offset
       : 421
1st Codon : 1
G H N R E S Y M V P F I P L Y R N G D F F I S S K D L G Y D
GGCCATAACAGAGAGTCCTACATGGTGCCTTTCATTCCCCTCTACAGAAACGGAGACTTTTTCATTAGCTCCAAGGATCTGGGATACGAT
        : Tyros
Segment# : 30
Offset
       : 436
1st Codon: 1
RNGDFFISSKDLGYDYSYLQDSDPDSFQDY
AGGAATGGCGATTTCTTTATCTCCAGCAAAGACCTCGGCTATGACTATAGCTATCTGCAAGACTCCGACCCTGACTCCTTCCAAGACTAT
        : Tyros
Segment# : 31
Offset
       : 451
1st Codon : 1
Y S Y L Q D S D P D S F Q D Y I K S Y L B Q A S R I W S W L
TACTCCTACCTCCAGGATAGCGATCCCGATAGCTTTCAGGATTACATTAAGTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCCTGGCTC
Gene
       : Tyros
Segment# : 32
Offset
       : 466
1st Codon : 1
I K S Y L E Q A S R I W S W L L G A A M V G A V L T A L L A
Gene
       : Tyros
```

161/216 Segment# : 33 Offset : 481 1st Codon : 1 LGAAMVGAVLTALLAGLVSLLCRHKRKQLP CTGGGAGCCGCTATGGTCGGCGCTGTGCTCACCGCTCTGCTCGCCGGACTGGTCAGCCTCCTGTGTAGGCATAAGAGAAAGCAACTGCCT : Tyros Segment# : 34 Offset : 496 1st Codon: 1 G L V S L L C R H K R K Q L P B B K Q P L L M B K B D Y H S GGCCTCGTGTCCCTGCTGCAGACACAAAAGGAAACAGCTCCCCGAAGAGAAACAGCCTCTGCTCATGGAAAAGGAAGACTATCACTCC : Tyros Segment# : 35 Offset : 511 1st Codon : 1 ERKQPLL M EKEDYH S L Y Q S H L A A GAGGAAAAGCAACCCCTCCTGATGGAGAAAGAGGATTACCATAGCCTCTACCAAAGCCATCTGGCTGCC : TRP2 Segment# : 1 Offset : 1 1st Codon : 1 AAMSPLWWGFLLSCLGCKILPGAQGQFPRV GCCGCTATGTCCCCCCTCTGGTGGGGCTTTCTGCTCAGCTGTCTGGGATGCAAAATCCTCCCCGGAGCCCAAGGCCAATTCCCTAGGGTC : TRP2 Gene Segment# : 2 : 16 1st Codon : 1 G C K I L P G A Q G Q P P R V C M T V D S L V N K E C C P R GGCTGTAAGATTCTGCCTGGCGCTCAGGGACAGTTTCCCAGAGTGTGTATGACAGTGGATAGCCTCGTGAATAAGGAATGCTGTCCCAGA Gene : TRP2 Segment# : 3 Offset : 31 1st Codon : 1 C M T V D S L V N K E C C P R L G A E S A N V C G S Q Q G R Gene : TRP2 Segment# : 4 Offset : 46 1st Codon : 1 L G A B S A N V C G S Q Q G R G Q C T B V R A D T R P W S G CTGGGAGCCGAAAGCGCTAACGTCTGCGGAAGCCAACAGGGAAGGGGACAGTGTTACCGAAGTGAGAGCCGATACCAGACCCTGGAGCGGA Gene : TRP2 Segment# : 5 Offset : 61 1st Codon : 1 G Q C T E V R A D T R P W S G P Y I L R N Q D D R B L W P R GGCCAATGCACAGAGGTCAGGGCTGACACAAGGCCTTGGTCCGGCCCTTACATTCTGAGAAACCAAGACGATAGGGAACTGTGGCCCAGA : TRP2 Gene Segment# : 6 : 76 PYILRNQDDRELWPRKFFHRTCKCTGNFAG CCCTATATCCTCAGGAATCAGGATGACAGAGAGCTCTGGCCTAGGAAATTCTTTCACAGAACCTGTAAGTGTACCGGAAACTTTGCCGGA : TRP2 Segment# : 7 Offset : 91 1st Codon : 1 K F F H R T C K C T G N F A G Y N C G D C K F G W T G P N C AAGTTTTTCCATAGGACATGCAAATGCACAGGCAATTTCGCTGGCTATAACTGTGGCGATTGCAAATTCGGATGGACAGGCCCTAACTGT

Gene : TRP2 Segment# : 8 Offset : 106

Figure 27 (Cont)

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1st Codon : 1 Y N C G D C K P G W T G P N C B R K K P P V I R Q N I H S L Gene : TRP2 Segment# : 9 1st Codon : 1 B R K K P P V I R Q N I H S L S P Q E R E Q F L G A L D L A Gene : TRP2 Segment# : 10 Offset 1st Codon : 1 S P Q B R B Q P L G A L D L A K R V H P D Y V I T T Q H W AGCCCTCAGGAAAGGGAACAGTTTCTGGGAGCCCTCGACCTCGCCAAAAAGAGAGTGCATCCCGATTACGTCATCACAACCCAACACTGG Gene : TRP2 Segment# : 11 Offset : 151 K K R V H P D Y V I T T Q H W L G L L G P N G T Q P Q F A N AAGAAAAGGTTCCACCCTGACTATGTGATTACCACACAGCATTGGCTCGGCCTCCTGGGACCCAATGGCACACAGCCTCAGTTTGCCAAT Gene : TRP2 Segment# : 12 Offset : 166 1st Codon : 1 LGLLGPNGTQPQFANCSVYDFPVWLHYYSV CTGGGACTGCTCGGCCCTAACGGAACCCCAACTCGCTAACTGTAGCGTCTACGATTTCTTTGTGTGGCTGCATTACTATAGCGTC Gene : TRP2 Segment# : 13 Offset : 181 C S V Y D F F V W L H Y Y S V R D T L L G P G R P Y R A I D TGCTCCGTGTATGACTTTTTCGTCTGGCTCCACTATTACTCCGTGAGAGACACTGCTCGGCCTGGCAGACCCTATAGGGCTATCGAT Segment# : 14 Offset : 196 1st Codon : 1 RDTLLGPGRPYRAIDPSHQGPAPVTWHRYH AGGGATACCCTCCTGGGACCCGGAAGGCCTTACAGAGCCATTGACTTTAGCCATCAGGGACCCGCTTTCGTCACCTGGCACAGATACCAT Gene : TRP2 Segment# : 15 Offset : 211 1st Codon : 1 F S H Q G P A F V T W H R Y H L L C L B R D L Q R L I G N B TTCTCCCACCAAGGCCCTGCCTTTGTGACATGGCATAGGTATCACCTCCTGTGTCTGGAAAGGGATCTGCAAAGGCTCATCGGAAACGAA : TRP2 Gene Segment# : 16 Offset : 226 1st Codon : 1 L L C L B R D L Q R L I G N B S F A L P Y W N F A T G R N R CTGCTCTGCCTCGAGAGAGACCTCCAGAGACTGATTGGCAATGAGTCCTTCGCTCTGCCTTACTGGAACTTTTGCCACAGGCAGAAACGAA Gene Segment# : 17 Offset S F A L P Y W N F A T G R N E C D V C T D Q L F G A A R P D : TRP2 Gene Segment# : 18 Offset : 256 1st Codon : 1 C D V C T D Q L P G A A R P D D P T L I S R N S R F S S W R

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TGCGATGTGTGTACCGATCAGCTCTTCGGAGCCGCTAGGCCTGACGATCCCACACTGATTAGCAGAAACTCCAGGTTTAGCTCCTGGGAA
        : TRP2
 Gene
 Segment# : 19
 Offset
        : 271
 1st Codon : 1
 D P T L I S R N S R P S S W E T V C D S L D D Y N H L V T L
 GACCCTACCCTCATCTCCAGGAATAGCAGATTCTCCAGCTGGGAGACAGTGTGTGACTCCCTGGATGACTATAACCATCTGGTCACCCTC
        : TRP2
 Gene
 Segment# : 20
 Offset
       : 286
 1st Codon : 1
 TVCDSLDDYNHLVTLCNGTYEGLLRRNQMG
 Gene
        : TRP2
 Segment# : 21
 Offset
 1st Codon : 1
 C N G T Y E G L L R R N Q M G R N S M K L P T L K D I R D C
 TGCAATGGCACATACGAAGGCCTCCTGAGAAGGAATCAGATGGGCAGAAACTCCATGAAACTGCCTACCCTCAAGGATATCAGAGACTGT
Gene
        : TRP2
Segment# : 22
Offset
       : 316
1st Codon : 1
 R N S M K L P T L K D I R D C L S L Q K F D N P P F P Q N S
Gene
       : TRP2
Segment# : 23
Offset
       : 331
1st Codon : 1
 LSLQKFDNPPFPQNSTFSFRNALEGFDKAD
CTGTCCCTGCAAAAGTTTGACAATCCCCCTTTCTTTCAGAATAGCACATTCTCCTTCAGAAACGCTCTGGAAGGCTTTGACAAAGCCGAT
Segment# : 24
Offset
       : 346
1st Codon : 1
 T F S F R N A L E G F D K A D G T L D S Q V M S L H N L V H
ACCTTTAGCTTTAGGAATGCCCTCGAGGGATTCGATAAGGCTGACGGAACCCTCGACTCCCAGGTCATGTCCCTGCATAACCTCGTGCAT
       : TRP2
Gene
Segment# : 25
Offset
       : 361
G T L D S Q V M S L H N L V H S F L N G T N A L P H S A A N
Gene
       : TRP2
Segment# : 26
Offset
       : 376
1st Codon : 1
S F L N G T N A L P H S A A N D P I F V V L H S F T D A I P
AGCTTTCTGAATGGCACAAACGCTCTGCCTCACTCCGCCGCTAACGATCCCATTTTCGTCGTCGTCCACTCCTTCACAGACGCTATCTTT
       : TRP2
Gene
Segment# : 27
Offset
      : 391
1st Codon : 1
D P I P V V L H S P T D A I F D E W M K R F N P P A D A W P
GACCCTATCTTTGTGGTCCTGCATAGCTTTACCGATGCCATTTTCGATGAGTGGATGAAAAGGTTTAACCCTCCCGCTGACGCTTGGCCT
       : TRP2
Gene
Segment# : 28
      : 406
Offset
1st Codon : 1
D B W M K R P N P P A D A W P Q B L A P I G H N R M Y N M V
GACGAATGGATGAAGAGATTCAATCCCCCTGCCGATGCCTGGCCCCAAGAGCTCGCCCCTATCGGACACAATAGGATGTACAATATGGTC
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Gene : TRP2 Segment# : 29 Offset : 421 1st Codon : 1 Q B L A P I G H N R M Y N M V P F P P V T N B B L P L T S : TRP2 Segment# : 30 Offset : 436 1st Codon : 1 P F F P P V T N E E L F L T S D Q L G Y S Y A I D L P V S V CCCTTTTTCCCTCCCGTCACCAATGAGGAACTGTTTCTGACAAGCGATCAGCTCGGCTATAGCTATGCCATTGACCTCCCCGTCAGCGTC : TRP2 Segment# : 31 Offset : 451 1st Codon : 1 ·DQLGYSYAIDLPVSVEETPGWPTTLLVVMG GACCAACTGGGATACTCCTACGCTATCGATCTGCCTGTGTCCGTGGAGAGACACCCCGGATGGCCTACCACACTGCTCGTCGTCATGGGA : TRP2 Gene Segment# : 32 : 466 1st Codon : 1 BETPGWPTTLLVVMGTLVALVGLPVLLAFL GAGGAAACCCCTGGCTGGCCCACAACCCTCCTGGTCGTGATGGGCACACTGGTCGCCCTCGTGGGACTGTTTGTGCTCCTGGCTTTCCTC Gene : TRP2 Segment# : 33 Offset : 481 1st Codon : 1 T L V A L V G L F V L L A F L Q Y R R L R K G Y T P L M E T ACCCTCGTGGCTCTGGTCGCCCTCTTCGTCCTGCTCGCCTTTTCTGCAATACAGAAGGCTCAGGAAAGGCTTATACCCCTCTGATGGAGACA : TRP2 Gene Segment# : 34 Offset : 496 1st Codon : 1 Q Y R R L R K G Y T P L M E T H L S S K R Y T E E A A A CAGTATAGGAGACTGAGAAAGGGATACACCCCTCATGGAAAACCCATCTGTCCAGCAAAAAGGTATACCGAAGAGGCTGCCGCT Gene Segment# : 1 A A M A V Q G S Q R R L L G S L N S T P T A I P Q L G L A A GCCGCTATGGCTGTGCAAGGCTCCCAGAGAAGGCTCCTGGGAAGCCTCAACTCCACCCCTACCGCTATCCCTCAGCTCGGCCTCGCCGCT Gene : MC1R Segment# : 2 Offset : 16 LNSTPTAIPQLGLAANQTGARCLEVSISDG CTGAATAGCACCCCACAGCCATTCCCCCAACTGGGACTGGCTGACCAGCCGGCTAGGTGTCTGGAAGTGTCCATCTCCCGACGGA : MClR Gene Segment# : 3 Offset : 31 1st Codon : 1 N Q T G A R C L E V S I S D G L F L S L G L V S L V E N A L AACCAAACCGGAGCCAGATGCCTCGAGGTCAGCATTAGCGATGGCCTCTTCCTCAGCCTCGGCCTCGTGTCCCTGGTCGAGAATGCCCTC Gene : MClR Segment# : 4 Offset 1st Codon : 1 L F L S L G L V S L V E N A L V V A T I A K N R N L H S P M CTGTTTCTGTCCCTGGGACTGGTCAGCCTCGTGGAAAACGCTCTGGTCGTGGCTACCATTGCCAAAAACAGAAACCTCCACTCCCCCATG Gene : MC1R Segment# : 5

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Offset : 61 1st Codon : 1 V V A T I A K N R N L H S P M Y C P I C C L A L S D L L V S GTGGTCGCCACAATCGCTAAGAATAGGAATCTGCATAGCCCTATGTATTGCTTTATCTGTTGCCCCCTCAGCGATCTGCTCGTGTCC : MC1R Gene Segment# : 6 Offset : 76 1st Codon : 1 Y C F I C C L A L S D L L V S G T N V L E T A V I L L E A TACTGTTTCATTTGCTGTCTGGCTCTGTCCGACCTCCTGGTCAGCGGAACCAATGTGCTCGAGACAGCCGTCATCCTCCTGCTCGAGGCT : MC1R Gene Segment# : 7 Offset : 91 1st Codon : 1 G T N V L E T A V I L L E A G A L V A R A A V L Q Q L D N GGCACAAACGTCCTGGAAACCGCTGTGATTCTGCTCCTGGAAGCCGGAGCCCTCGTGGCTAGGGCTGCCGTCCTGCAACAGCTCGACAAT : MC1R Gene Segment# : 8 Offset : 106 1st Codon : 1 G A L V A R A A V L Q Q L D N V I D V I T C S S M L S S L C GGCGCTCTGGTCGCCAGAGCCGCTGTGCTCCAGCAACTGGATAACGTCATCGATGTGATTACCTGTAGCTCCATGCTCAGCTCCCTGTGT : MC1R Gene Segment# : 9 Offset : 121 1st Codon : 1 V I D V I T C S S M L S S L C F L G A I A V D R Y I S I F Y GTGATTGACGTCATCACATGCTCCAGCATGCTGTCCAGCCTCTGCTTTCTGGGAGCCATTGCCGTCGACAGATACATTAGCATTTTCTAT Gene Segment# : 10 Offset : 136 1st Codon : 1 F L G A I A V D R Y I S I F Y A L R Y H S I V T L P R A P R TTCCTCGGCGCTATCGCTGTGGATAGGTATATCTCCATCTTTTACGCTCTGAGATACCATAGCATTGTGACACTGCCTAGGGCTCCCAGA : MC1R Gene Segment# : 11 Offset : 151 1st Codon : 1 A L R Y H S I V T L P R A P R A V A A I W V A S V V F S T L GCCCTCAGGTATCACTCCATCGTCACCCTCCCCAGAGCCCCTAGGGCTGTGGCTGCCATTTGGGTCGCCTCCGTGGTCTTCTCCACCCTC Gene : MC1R Segment# : 12 Offset : 166 1st Codon : 1 A V A A I W V A S V V F S T L F I A Y Y D H V A V L L C L V GCCGTCGCCGCTATCTGGGTGGCTAGCGTCGTGTTTAGCACACTGTTTATCGCTTACTATGACCATGTGGCTGTGCTCCTGTGTCTGGTC : MC1R Gene Segment# : 13 Offset : 181 1st Codon : 1 FIAYYD H V A V L L C L V V F F L A M L V L M A V L Y V TTCATTGCCTATTACGATCACGTCGCCGTCCTGCTCGTCGTCGTCTTCTTCTGGCTATGCTCGTGCTCATGGCTGTGCTCTACGTC : MC1R Gene Segment# : 14 Offset : 196 1st Codon : 1 V F F L A M L V L M A V L Y V H M L A R A C Q H A Q G I A R GTGTTTTTCCTCGCCATGCTGGTCCTGATGGCCGTCCTGTATGTGCATATGCTCGCCAGAGCCTGTCAGCATGCCCAAGGCATTGCCAGA : MCIR Gene Segment# : 15 Offset : 211 1st Codon : 1

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H M L A R A C Q H A Q G I A R L H K R Q R P V H Q G F G L K CACATECTGGCTAGGGCTTGCCAACACGCTCAGGGAATCGCTAGGCTCCACAAAAGGCAAAGGCCTGTGCATCAGGGATTCGGACTGAAA : MC1R Gene Segment# : 16 Offset : 226 1st Codon : 1 LHKRQRPVHQGPGLKGAVTLTILLGIPFLC Gene : MC1R Segment# : 17 Offset : 241 1st Codon : 1 G A V T L T I L L G I F F L C W G P F P L H L T L I V L C P : MC1R Gene Segment# : 18 Offset : 256 1st Codon : 1 W G P F F L H L T L I V L C P B H P T C G C I F K N F N L F TGGGGACCCTTTTTCCTCCACCTCACCTCATCGTCCTGTGTCCCGAACACCCTACCTGTGGCTGTATCTTTAAGAATTTCAATCTGTTT Gene : MC1R Segment# : 19 Offset : 271 1st Codon : 1 B H P T C G C I F K N F N L F L A L I I C N A I I D P L I Y GAGCATCCCACATGCGGATGCATTTTCAAAAACTTTAACCTCTTCCTCGCCCTCATCATTTGCAATGCCATTATCGATCCCCTCATCTAT Segment# : 20 Offset : 286 1st Codon : 1 LALIICNAIIDPLIXAFHSQELRRTLKEVL CTGGCTCTGATTATCTGTAACGCTATCATTGACCCTCTGATTTACGCTTTCCATAGCCAAGAGCTCAGGAGAACCCTCAAGGAAGTGCTC Gene : MC1R Segment# : 21 : 301 Offset 1st Codon : 1 AFHSQELRRTLKEVLTCSWAA GCCTTTCACTCCCAGGAACTGAGAAGGACACTGAAAGAGGTCCTGACATGCTCCTGGGCTGCC : MUCLP Gene Segment# : 1 Offset 1st Codon : 1 A A M T P G T Q S P F F L L L L T V L T V V T G S G H A S GCCGCTATGACACCCGGAACCCAAAGCCCTTTCTTCTGCTCCTGCTCCTGACAGTGCTCACCGTCGTGACAGGCTCCGGCCATGCCTCC Gene : MUC1F Segment# : 2 Offset : 16 1st Codon : 1 L L T V L T V V T G S G H A S S T P G G E K E T S A T Q R S CTGCTCACCGTCCTGACAGTGGTCACCGGAAGCGGACACGCTAGCTCCACCCCTGGCGGAGAGAAAGAGACAAGCGCTACCCAAAGGTCC : MUC1F Gene Segment# : 3 Offset : 31 1st Codon : 1 STPGGEKETSATQRSSVPSSTEKNAVSMTS AGCACACCGGAGGCGAAAAGGAAACCTCCGCCACACAGAGAAGCTCCGTGCCTAGCTCCACCGAAAAGAATGCCGTCAGCATGACCTCC seme : MUCIF Segment# : 4 : 46 Offset · 1st Codon : 1 S V P S S T B K N A V S M T S S V L S S H S P G S G S S T T AGCSTCCCCTCCAGCACAGAGAAAAACGCTGTGTCCATGACAAGCTCCGTGCTCAGCTCCCCCCGGGAAGCGGAAGCTCCACCACA

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: MUC1P Segment# : 5 Offset : 61 1st Codon : 1 S V L S S H S P G S G S S T T Q G Q D V T L A P A T B P A S Gene : MUC1F Segment# : 6 : 76 Offset 1st Codon : 1 Q G Q D V T L A P A T E P A S G S A A T W G Q D V T S V P V CAGGGACAGGATGTGACACTGGCTCCCGCTACCGAACCCGCTAGCGGAAGCGCTGCCACATGGGGACAGGATGTGACAAGCGTCCCCGTC Gene : MUC1F Segment# : 7 Offset : 91 1st Codon : 1 G S A A T W G Q D V T S V P V T R P A L G S T T P P A H D V GGCTCCGCCGCTACCTGGGGCCAAGACGTCACCTCCGTGCCTGTGACAAGGCCTGCCCTCGGCTCCACCACACCCCCTGCCCATGACGTC Gene : MUC1F Segment# : 8 Offset : 106 1st Codon : 1 TRPALGSTTPPAHDVTSAPDNKAA ACCAGACCCGCTCTGGGAAGCACAACCCCTCCCGCTCACGATGTGACAAGCGCTCCCGATAACAAGCCGCT : MUC1R Segment# : 1 1st Codon : 1 A A N R P A L G S T A P P V H N V T S A S G S A S G S A S T GCCGCTAACAGACCCGCTCTGGGAAGCACAGCCCCTCCCGTCCACAATGTGACAAGCGCTAGCGGAAGCGCTAGCGGAAGCGCTAGCACA Gene : MUC1R Segment# : 2 Offset : 16 1st Codon : 1 N V T S A S G S A S G S A S T L V H N G T S A R A T T T P A : MUC1R Gene Segment# : 3 Offset : 31 1st Codon : 1 L V H N G T S A R A T T T P A S K S T P P S I P S H H S D T CTGGTCCACAATGGCACAAGGGCTAGGGCTACCACAACCCCTGCCTCCAAGTCCACCCCTTTCTCCATCCCTAGGCATCACTCCGACACA Gene : MUC1R ... Segment# : 4 Offset : 46 1st Codon: 1 SKSTPFSIPSHHSDTPTTLASHSTKTDASS Segment# : 5 : 61 Offset 1st Codon : 1 P T T L A S H S T K T D A S S T H H S S V P P L T S S N H S : MUC1R Segment# : 6 Offset. : 76 1st Codon : 1 THHSS V P P L T S S N H S T S P Q L S T G V S F F P L S Gene : MUC1R

168/216 Segment# : 7 Offset : 91 1st Codon : 1 T S P Q L S T G V S F F F L S F H I S N L Q F N S S L E D P ACCTCCCCCAACTGTCCACCGGAGTGTCCTTCTTTTTCCTCAGCTTTCACATTAGCAATCTGCAATTCAATAGCTCCCTGGAAGACCCT : MUC1R Gene Segment# : 8 Offset : 106 1st Codon : 1 FHISNLQFNSSLEDPSTDYYQELQRDISEM TTCCATATCTCCAACCTCCAGTTTAACTCCAGCCTCGAGGATCCCTCCACCGATTACTATCAGGAACTGCAAAGGGATATCTCCGAGATG Gene : MUC1R Segment# : 9 : 121 Offset 1st Codon : 1 S T D Y Y Q B L Q R D I S E M F L Q I Y K Q G G F L G L S N AGCACAGACTATTACCAAGAGCTCCAGAGAGACATTAGCGAAATGTTTCTGCAAATCTATAAGCAAGGCGGATTCCTCGGCCTCAGCAAT : MUC1R Gene Segment# : 10 Offset : 136 1st Codon : 1 PLQIYKQGGFLGLSNIKFRPG/SVVVQLTLA TTCCTCCAGATTTACAAACAGGGAGGCTTTCTGGGACTGTCCAACATTAAGTTTAGGCCTGGCTCCGTGGTCGTGCAACTGACACTGGCT : MUCIR Gene Segment# : 11 Offset : 151 1st Codon: 1 IK P R P G S V V Q L T L A F R B G T I N V H D V B T Q F : MUC1R Segment# : 12 Offset 1st Codon : 1 FREGTINVHDVETQFNQYKTEAASRYNLTI TTCAGAGAGGGAACCATTAACGTCCACGATGTGGAAACCCCAATTCAATCAGTATAAGACAGAGGCTGCCTCCAGGTATAACCTCACCATT : MUC1R Gene Segment# : 13 Offset : 181 1st Codon : 1 N Q Y K T B A A S R Y N L T I S D V S V S D V P F P F S A Q AACCAATACAAAACCGAAGCCGCTAGCAGATACAATCTGACAATCTCCGACGTCAGCGTCAGCGATGTGCCTTTCCCTTTCTCCGCCCAA : MUC1R Gene Segment# : 14 Offset : 196 1st Codon : 1 S D V S V S D V P F P F S A Q S G A G V P G W G I A L L V L AGCGATGTGTCCGTGTCCGACGTCCCCTTTCCCTTTAGCGCTCAGTCCGGCGCTGGCGGTCCCCGGATGGGGAATCGCTCTGCTCCTGCTC : MUC1R Gene Segment# : 15 Offset : 211 1st Codon : 1 S G A G V P G W G I A L L V L V C V L V A L A I V Y L I A L AGCGGAGCCGGAGTGCCTGGGGGCATTGCCCTCCTGGTCTGGTCTGGTCCTGGTCCTGGTCCCCATTGTGTATCTGATTGCCCTC Gene : MUC1R Segment# : 16 Offset : 226 1st Codon : 1 V C V L V A L A I V Y L I A L A V C Q C R R K N Y G Q L D I

: MUC1R Gene Segment# : 17 Offset : 241

Figure 27 (Cont)

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1st Codon : 1

A V C Q C R R K N Y G Q L D I F P A R D T Y H P M S B Y P T GCCGTCTGCCAATGCAGAAGGAAAAACTATGGCCAACTGGATATCTTTCCCGCTAGGGATACCTATCACCCTATGTCCGAGTATCCCACA

Gene : MUC1R Segment# : 18 Offset : 256 1st Codon : 1

Gene : MUC1R Segment# : 19 Offset : 271 1st Codon : 1

Y H T H G R Y V P P S S T D R S P Y E K V S A G N G G S S L TACCATACCCATGGCAGATACGTCCCCCTAGGCTCCACCGATAGGTCCCCCCTATGAGAAAGTGTCCGCCGGAAACGGAGGCTCCAGCCTC

Gene : MUC1R Segment# : 20 Offset : 286 1st Codon : 1

S P Y B K V S A G N G G S S L S Y T N P A V A A A S A N L A AGCCCTTACGAAAAGGTCAGCGCTGGCGGAAGGTCCCTGTCCTACACAAACCCTGCCGTCGCCGCTGCCCCCAATCTGGCT

Gene : MUC1R
Segment# : 21
Offset : 301
1st Codon : 1

S Y T N P A V A A A S A N L A A AGCTATACCAATCCCGCTGTGGCTGCCGCTAGCGCTAACCTCGCCGCT

Segments in scrambled order:

gp100 #4

W N R Q L Y P E W T B A Q R L D C W R G G Q V S L K V S N D
TGGAATAGGCAACTGTATCCCGAATGGACAGAGGCTCAGAGACTGGATGCTGGAGGGGAGGCCAAGTGTCCCTGAAAGTGTCCCAACGAT

TRP2 #6

Tyros #30

RNGDFFISSKDLGYDYSYLQDSDPDSFQDY AGGAATGCCGATTTCTTTATCTCCAGCAAAGACCTCGGCTATGACTATAGCTATCTGCAAGACTCCGACCCTGACCCCTTCCAAGACTAT

TRP-1 #1

A A P A F L T W H R Y H L L R L E K D M Q E M L Q E P S F S GCCGCTCCCGCTTTCCTCACCTGGCACAGATACCATCTGCTCAGGCTCGAGAAAGACATCCAGGAAATGCTCCAGGAACCCTCCTTCTCC

Tyros #29

GHNRESYMVPFIPLYRNGDFFISSKDLGYD GGCCATAACAGAGAGTCCTACAGTGCCTTTCATTCCCCTCTACAGAAACGGAGACTTTTTCATTAGCTCCAAGGATCTGGGATACGAT

TRP2 #16

LLCLBRDLQRLIGNBSFALPYWNFATGRNECTGCTCTGCCTCGCAGAGAGACGAAACGAA

gp100 #23

T T E V V G T T P G Q A P T A E P S G T T S V Q V P T T E V
ACCACAGAGGTCGTGGGAACCCACACCCGGACAGGGTCCCACAGAGGTC

MUC1R #9

gp100 #36

A C M B I S S P G C Q P P A Q R L C Q P V L P S P A C Q L V GCCTGTATGGAAATCTCCAGCCTGGCTGCCAGCCTCCGGCTCAGAGACTGTGTCAGCCTGTCCTGCCCCCCCGCTTGCCAACTGGTC

TRP2 #31

D Q L G Y S Y A I D L P V · S V E E T P G W P T T L L V V M G

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GACCAACTGGGATACTCCTACGCTATCGATCTGCCTGTGTCCGTGGAAGAGACACCCGGATGGCCTACCACACTGCTCGTGGTCATGGGA

TRP-1 #7

T E D G P I R R N P A G N V A R P M V Q R L P E P Q D V A Q ACCGAAGACGCCATTAGGAGAAACCCTGCCGGAAACGTCGCCCAAGACCCCATGGTGCAAAGGCTCCCCGAACCCCCAAGACGTCGCCCAA

TRP2 #3

WUC1R #13

NQYKTBAASRYNLTISDVSVSDVPPPPSAQ AACCAATACAAAACCGAAGCCGCTAGCAGATACAATCTGACAATCTCGGACGTCAGCGTCAGCGATGTGCCTTTCCCTTTCTCCGCCCAA

TRP2 #1

A A M S P L W W G F L L S C L G C K I L P G A Q G Q F P R V GCCGCTATGTCCCCCGGAGCCCAAGGCCAATTCCCTAGGGTC

gp100 #18

qp100 #27

LABMSTPBATGMTPAEVSIVVLSGTTAAQVCTGGCTGAGATGACCACAGCCGCAGGCCTCAGGTC

MUC1R #11

MUCLF #7

G S A A T W G Q D V T S V P V T R P A L G S T T P P A H D V GGCTCCGCCCTACCTCGCCCACACCCCCTCCCCATGACGTC

MC1R #16

MC1R #20

LALIICNAIIDPLIYAFHSQELRRTLKEVL CTGGCTCTGATTATCTGTAACGCTATCATTGACCCTCTGATTTACGCTTTCCATAGCCAAGAGCTCAGGAGAACCCTCAAGGAAGTGCTC

TRP2 #

K F P H R T C K C T G N F A G Y N C G D C K F G W T G P N C AAGTTTTTCCATAGGACAGGATGCAAATTCGGATGCAAATTCGGATGGACAGCCCTAACTGT

TRP2 #23

L S L Q K P D N P P F F Q N S T F S P R N A L E G F D K A D CTGTCCCTGCAAAGTTTGACAATCCCCTTTCTTTCAGAATAGCACTTCTCCTTCAGAAACGCTCTGGAAGGCTTTGACAAAGCCGAT

MUCIR #4

MUCIR #1

A A N R P A L G S T A P P V H N V T S A S G S A S G S A S T GCCGCTAACAGCCCCTCTCGGCAAGCCCCTCCCGTCCACAATGTGACAAGCGCTAGCGGGAAGCGCTAGCGGAAGCGCTAGCACA

TRP2 #21

C N G T Y E G L L R R N Q M G R N S M K L P T L K D I R D C TGCAATGGCACATACGAAGGCCTCCTGAGAAGGAATCAGATGGCCACAAACTCCATGAAACTGCCTCAAGGATATCAGAGACTGT

MIICIR #4

MC1R #13

FIAYYDHVAVLLCLVVFFLAMLVLMAVLYV

Tyros #16

K L T G D E N P T I P Y W D N R D A E K C D I C T D E Y M G

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AAGCTCACCGGAGACGAAAACTTTACCATTCCCTATTGGGATTGGAGAGACGCTGAGAAATGCGATATCTGTACCGATGAGTATATGGGA

gp100 #32

L R L V K R Q V P L D C V L Y R Y G S F S V T L D I V Q G I CTGAGACTGGTCAAGAGACAGGTCCCCTCGACTGTGTGCTCTACAGATACGGAAGCTTTAGCGTCACCCTCGACATTGTGCAAGGCATT

MUCLR #10

PLQIYKQGGPLGLSNIKFRPGSVVVQLTLA

MC1R #9

V I D V I T C S S M L S S L C F L G A I A V D R Y I S I F Y GTGATTGACGTCATCACATGCTCCAGCATGCTCTCTGCTTTCTGGGAGCCATTGCCGTCGACAGATACATTAGCATTTTCTAT

Tyros #21

RNPGNHDKSRTPRLPSSADVBPCLSLTQYBAGGAAACCCAGAAAAGCAGAAACCCAGAAAACCAAAAAGCAGAAACCCCTAGGCTCCCCTCCAGCGCTGACGTCTGAGTTTTGCCTCAGCCTCACCCAATACGAA

TRP-1 #14

gp100 #39

V S L A D T N S L A V V S T Q L I M P G Q B A G L G Q V P L GTGTCCCTGGCTGACACACACCCCCTGGCTGGCTCAGCACACACCCCCGGACAGGAACCCCGGACAGGTCCCCCTC

gp100 #20

G P V T A Q V V L Q A A I P L T S C G S S P V P G T T D G H
GGCCCTGTGACAGCCCAAGTGGTCCTGCAAGCCGCTTTGCCTACAAGCTGTGGCTCCAGCCCTTTGCCTGCACAACCGATGGCCAT

Tyros #8

K F G F W G P N C T E R R L L V R R N I F D L S A P E K D K AAGTITGGCTTTTGGGGACCCAATTGCACAGAGAAGACCACTCTGGTCAGGAGAACAAA

gp100 #13

L G T H T M E V T V Y H R R G S R S Y V P L A H S S S A F T CTGGGAACCCATACCATGGAGGTCACCATAGCTCCAGCGCTTTCACA

MCLR #12

TRP2 #25

G T L D S Q V M S L H N L V H S F L N G T N A L P H S A A N GGCACACTGGATAGCCAAGTGACGAACTGACCACTAGCGCTCCACAATCTGGTCCACTCCTCACAGCGAACCAATGCCCTCCCCCATAGCGCTGCCAAT

MART #4

G C W Y C R R R N G Y R A L M D K S L H V G T Q C A L T R R GGCTGTTGGTATTGCAGAAGGAGAAACGGATACAGAGGCCCTCATGGATAAGTCCCTGCATGTGGGAACCCAATGCGCTCTGACAAGGAGA

Tyros #15

PWHRLFLLRWEQEIQKLTGDENFTIPYWDW

MC1R #1

A A M A V Q G S Q R R L L G S L N S T P T A I P Q L G L A A GCCGCTATGGCTGGCAGGGCTCCCGGAGGCTCCCGGCTCACCCCTACCGCTATCCCTCAGCTCGGCTCGCCGCT

MCIR #5

V V A T I A K N R N L H S P N Y C F I C C L A L S D L L V S GTGGTCGCCACAATCGCTAAGAATAGGAATCTGCATAGCCCTATGTATTGCTTTATCTGTTGCCTCGCCCTCAGCGATCTGCTCGTTCCC

Tyros #25

QSSMHNALHIYMNGTMSQVQGSANDPIFLL CAGTCCAGCATGCACCTCCACATTTACATGAACGGAACCATGAGCCAAGTGCAAGGCTCCGCCAATGACCCTATCTTTCTGCTC

Tyros #18

G Q H P T N P N L L S P A S F F S S W Q I V C S R L E E Y N GGCCAACACCCTACCAATCCCAATCTGCTCAGCCTCGCCTCCTTCTTTAGCTCCTGGCAAATCGTCTGCTCCAGGCTCGAGGAATACAAT

MC1R #6

Y C P I C C L A L S D L L V S G T N V L E T A V I L L E A

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TACTGTTTCATTTGCTGTCTGGCTCTGTCCGACCTCCTGGTCAGCCGAACCAATGTGCTCGAGACAGCCGTCATCCTCCTGCTCGAGGCT

TRP2 #19

DPTLISRNSRFSSWETVCDSLDDYNHLVTLGACCCTCACCCTCATCTCCAGGAATAGCAGATTCTCCAGCTGGGAGACAGTGTGGACTCCCTGGATGACTATAACCATCTGGTCACCCTC

WCIP #8

TRPALGSTTPPAHDVTSAPDNKAA
ACCAGACCCGCTCTGGGAAGCAGCCCTCCCGCTCACGATGTGACAAGCGCTCCCGATAACAAGCCGCT

Tyros #17

R D A E K C D I C T D E Y M G G Q H P T N P N L L S P A S F AGGGATGCCGAAAAGTGTGGACATTTGCACAGACGAATACATGGGCGGACAGCATCCCACAAACCCTAACCTCCCCCGCTAGCTTT

qp100 #17

T P A L Q L H D P S G Y L A B A D L S Y T W D P G D S S G T ACCTITECCCTCCAGCTCCACGATCCCTCCGGCTATCTGGCTGAGGCTGACCTCAGCTATACCTGGGACTTTGGCGATAGCTCCGGCACA

Tyros #22

S S A D V B F C L S L T Q Y B S G S M D K A A N F S F R N T AGCTCCGCCGATGTGGATTCTCTTCTTCTCTCAGAAACACA

gp100 #6

G P T L I G A N A S P S I A L N P P G S Q K V L P D G Q V I
GGCCCTACCCTCATCGGAGCCAATGCCTCCTCCTCCCTCGATTTCCCTGGCTCCCAGAAAGTGCTCCCCGATGGCCAAGTGATT

MC1R #18

W G P F F L H L T L I V L C P B H P T C G C I F K N F N L P TGGGGACCCTTTTTCCTCCACCTCACCTCATCGTCCTGTGTCCCGAACACCCTACCTGTGCTGTGTCTTTAAGAATTTCAATCTGTTT

Tyros #7

CQCSGNFMGFNCGNCKFGPWGPNCTBRRLLTGCCAATGCTCCGGCCATTCTGGGCCCTAACTGTACCGAAAGGAGACTGCTC

TRP2 #34

Q Y R R L R K G Y T P L M E T H L S S K R Y T E E A A CAGTATAGGAGACTGAGAAAGGGATACACCCCCTCATGGAAACCCCATCTGTCCAGCAAAAGGTATACCGAAGAGGCTGCCGCT

TRP-1 #15

PLENAPIGHNRQYNMVPFWPPVTNTEMFVT

ap100 #7

N F P G S Q K V L P D G Q V I W V N N T I I N G S Q V W G G AACTITCCCGGAAGCCCAAAAGGTCCTGCCTGACGGACAGGTCATCTGGGTGATAACACAATCATTAACGGAAGCCCAAGTGTGGGGCGGA

gp100 #22

RPTABAPNTTAGQVPTTEVVGTTPGQAPTA

MUCLE #3

S T P G G E K B T S A T Q R S S V P S S T B K N A V S M T S AGCACCCGGAGGCGGAAAAGGAACCTCCGCCACACAGAGAAGCTCCGTCACCGAAAAGAATGCCGTCAGCATCACCTCC

gp100 #42

LIYRRRLMKQDPSVPQLPHSSSHWLRLPRI CTGATTTACAGAAGGAGCTGAAGACTTTAGCGTCCCCAACTGCCTCACTCCAGCTCCCACTGCCTGAGACTGCCTAGGATT

ר# כספת

L G L L G P N G T Q P Q F A N C S V Y D F F V W L H Y Y S V CTGGGACTGCTCACGGACTCCTAACGGAACCCCAACTCGCTAACTGTAGCGTCTACGATTTCTTTGTGTGGCTGCATTACTATAGCGTC

TRP-1 #9

C L E V G L P D T P P F Y S N S T N S F R N T V B G Y S D P TGCCTCGAGGCTCTTCGATACCCCTCCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCT

qp100 #1

A A M D L V L K R C L L H L A V I G A L L A V G A T K V P R GCCGCTATGGATCTGGTTCCTGAAAAGGTCCCCCACCCTCGCCGTCATCGGAGCCCTCCTCGCTGTGGGAGCCCACAAAGGTCCCCCAGA

MC1R #3

N Q T G A R C L E V S I S D G L F L S L G L V S L V E N A L

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 ${\tt AACCAAACCGGAGCCAGATGCCTCGAGGTCAGCATTAGCGATGGCCTCTTCCTCAGCCTCGGCCTCGTGTCCCTGGAGAATGCCCTC}$

Tyros #23

S G S M D K A A N F S F R N T L B G F A S P L T G I A D A S AGGGGAAGCATGGCGCTAACTTTAGCTTTAGGAATACCCTCGAGGGATTCGCTAGCCCTCTGACAGGCATTGCCGATGCCTCC

Tyros #4

SPCGQLSGRGSCQNILLSNAPLGPQPPFTG

Tyros #13

M H Y Y V S M D A L L G G S B I W R D I D F A H B A P A F L ATGCATTACTATGTGTCCATGGATGCCCTCCTGGGAGGCTCCGAGATTTGGAGAGACATTGACTTTGCCCATGAGGCTCCCGCTTTCCTC

Tyros #35

TRP2 #5

GQCTEVRADTRPWSGPYILRNQDDRBLWPR GGCCAATGCACAGAGGTCAGGGCTGACACAGGGCCTTGGCCCAGAAACCAAGACGATAGGGAACTGTGGCCCAGA

MUC1F #4

S V P S S T E K N A V S M T S S V L S S H S P G S G S S T T AGCGTCCCCTCCAGCACAGAGAAAAAACGCTGTGTCCATGACAAGCTCCTTGTGTCATGACAAGCTCCTTGTTCCATGACAAGCTCCCCCGGAAGCGGAAGCTCCACCACA

Tyros #12

T P M F N D I N I Y D L F V W M H Y Y V S M D A L L G G S E ACCCCTATGITTACGATATCAATATCTATGACCTCTCGTCTGGATGCACTATTACGTCAGCATGGACGCTCTGCTCGGCGGAAGCGAA

gp100 #9

QPVYPQETDDACIPPDGGPCPSGSWSQKRS CAGCCTGTGTATCCCCAAGAGAGACGACGACGCTGTATCTTTCCCGATGGGGGACCCTGTCCCTCGGCTCCTGGTCCCAGAAAAGGTCC

TRP-1 #6

D S L B D Y D T L G T L C N S T E D G P I R R N P A G N V A GACTCCCTGGAAGACTATGACACACTGGGAACCCTCTGCAATAGCACAGAGGATGGCCCTATCAGAAGGAATCCCGCTGGCAATGTGGCT

qp100 #8

W V N N T I I N G S Q V W G G Q P V Y P Q E T D D A C I F P TGGGTCAACAATACCATTATCAATGGCTCCCAGGTCTGGGGAGGCCAACCCGTCTACCCTCAGGAAACCGATGACGCTTGCATTTTCCCT

MART #

cm100 #14

SRSYVPLAHSSSAFTITDQVPFSVSVSQLR AGCAGAAGCTATGTGCCTCTGGCTCAGCTCCGCCTTTACCATTACCATTACCGTCAGCTCCCCTTTAGCGTCAGCGTCAGCCTCAGCCAACTGAGA

TRP-1 #:

LEKDMQEMLQEPSFSLPYWNFATGKNVCDI CTGGAAAAGGATATGCAAGAGATGTGTGTGACATT

TPD-1 #16

V P F W P P V T N T E M F V T A P D N L G Y T Y E A A GTGCCTTTCTGGCCCCTGTGACAAACACAGAGATGTTCGTCACCGCTCCCGATAACCTCGGCTATACCTATGAGGCTGCC

TRP2 #13

C S V Y D P F V W L H Y Y S V R D T L L G P G R P Y R A I D TGCTCCGTGTATGACTTTTTCTCTGGGTCCACTATTACTCCGTGAGAGACACTGCTCGGCCCTGGCAGACCCTATAGGGCTATCGAT

Tvros #9

VRRNIFDLSAPEKDKFFAYLTLAKHTISSD GTGAGAAGGAATATCTTTGACCTCAGCGCTCCCGAAAAGGATAAGTTTTTCGCTTACCTCACCCTCGCCAAACACACAATCTCCAGCGAT

MART #2

K K G H G H S Y T T A E E A A G I G I L T V I L G V L L I AAGAAAGGCCATGGCCATAGCTATACCACAGCCGAAGAGGCTGCCGGAATCGGAATCCTCATCCTCATCCTCGCGTCCTGCTCCTGATT

qp100 #11

PVYVWKTWGQYWQVLGGPVSGLSIGTGRAM

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TTCGTCTACGTCTGGAAAACCTGGGGCCCAATACTGGCAGGTCCTGGGAGGCCCTGTGTCCGGCCTCAGCATTGGCACAGGCAGAGCCATG

gp100 #12

mol00 #25

Tyros #19

PSSWQIVCSRLEBYNSHQSLCNGTPEGPLRTTCTCCAGCTGCAGATTGTGTGTAGCAGACTGGAAGAGTATAACTCCCACCAAAGCCTCTGCAATGGCACACCCGAAGGCCCTCTGAGA

TRP2 #27

DPIPVVLHSFTDAIPDEWMKRFNPPADAWPGACCCTATCTTTGTGGTCCTGCATAGCTTTACCGTTGCCTTTCGATGAGTGAAAAGGTTTAACCCTCCCGCTGACGCTTGGCCT

MC1R #15

H M L A R A C Q H A Q G I A R L H K R Q R P V H Q G F G L K CACATGCTGGCTTGCCAACACGCTCAGGGAATCGCTGGGCTCCACAAAAGGCCAAGGCCTGTGCATCAGGGATTCGGACTGAAA

MUCLF #2

L L T V L T V V T G S G H A S S T P G G E K E T S A T Q R S CTGCTCACCGTCCTGACAGTGGTCACCGGAAGGGCACAGCGCTACCCAAAGGTCC

gp100 #44

F C S C P I G E N S P L L S G Q Q V A A
TTCTGTAGCTGTCCCATTGGCGAAAACTCCCCCTCCTGTCCGGCCAACAGGTCGCCGCT

TRP2 #24

T P S P R N A L E G P D K A D G T L D S Q V M S L H N L V H ACCTTTAGCTTTAGGAATGCCCTCGAGGGATTCGATAACCTCGTGCAT ACCTTTAGCTTTAGGAATGCCCTCGAGGGAACCCTCGACTCCCAGGTCATGTCCCTGCATAACCTCGTGCAT

Tyros #20

SHQSLCNGTPEGPLRRNPGNHDKSRTPRLPAGCCATCAGTCCCTGTGAACGCCCTGAGGGCACCCCTCAGGAGAACCCTTGGCAATCACGATAAGTCCAGGACACCCAGACTGCCT

TRP2 #30

PFFPPVTNEBLFLTSDQLGYSYAIDLPVSVCCCTTTTTCCCTCCCGTCACCAATGAGGAACTGTTTCTGACAAGCGATCAGCTCGGCTATAGCTATGCCATTGACCTCCCCGTCAGCGTC

TPP2 #9

TRP2 #29

Q E L A P I G H N R M Y N M V P F F P P V T N E E L F L T S CAGGAACTGGCCCCCATGGCCATAACGAAGAGTGTATAACATGGTGCCTTCTTCCCCCTGTGACAAACGAAGAGCTCTTCCTCACCTCC

gp100 #28

MUCIR #7

T S P Q L S T G V S F F F L S F H I S N L Q F N S S L E D P ACCTCCCCCAACTGTCCACCGGGGGGGCCCTTCTTTTTCCTCAGCTTTCACATTAGCAACTCTGCAATTCAATAGCTCCCTGGAAGACCCT

MUC1R #19

YHTHGRYVPPSSTDRSPYBKVSAGNGGSSL TACCATACCCATGGCAGATACGTCCCCCTAGCTCCACCGATAGGTCCCCCTATGAGAAAGTGTCCGCCGGAAACGGAGGCTCCAGCCTC

MC1 D #4

L P L S L G L V S L V B N A L V V A T I A K N R N L H S P M CTGTTTCTGTCCCTGGGACTGGCTCGTGGAAAACGCTCTGGTCGTGGCTGCCATGCCAAAAACAGAAACCTCCACTCCCCCATG

TRP2 #26

S F L N G T N A L P H S A A N D P I F V V L H S P T D A I F AGCTTTCTGAATGGCACAAACGCTCTGCCTCACTCGCCGCTAACGATCCCATTTTCGTCGTGCTCCACTCCTTCACAGACGCTATCTTT

WC1R #17

AVCQCRRKNYGQLDIFPARDTYHPMSEYPT

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GCCGTCTGCCAATGCAGAAGGAAAAACTATGGCCAACTGGATATCTTTCCCGCTAGGGGATACCTATCACCCTATGTCCGAGTATCCCACA

MC1R #14

V F F L A M L V L M A V L Y V H M L A R A C Q H A Q G I A R GTGTTTTTCCTCGCCATGCTGGTCCTGATGGCCGTCTGTATGTGCATATGCTCGCCAGAGCCTGTCAGCATGCCCAAGGCATTGCCAGA

TRP-1 #10

S T N S F R N T V E G Y S D P T G K Y D P A V R S L H N L A AGCACAAACTCCTTCAGAAACACAGTGGAAGGCTATAGGGTTCCCACAGGCAAATCCGGTTGAGAAGCCTCCACAATCTGGCT

TRP-1 #3

L P Y W N F A T G K N V C D I C T D D L M G S R S N F D S T CTGCCTTACTGGAACTTTGCCACAGGCAAAAACGTCTGCGATATCTGTACCGATGACCTCATGGGAAGCAAGAAGCAATTTCGATAGCACA

ap100 #19

MUCLR #8'

MUC1R #20

S P Y E K V S A G N G G S S L S Y T N P A V A A A S A N L A AGCCCTTACGAAAAGGTCAGCGCTGCCGCAATCTGGCT

Tyros #11

gp100 #37

gp100 #33

RYGSPSVTLDIVQGIBSAEILQAVPSGEGD AGGTATGGCTCCTTCTCCGTGACACTGGATATCGTCCAGGGATCGAAAGCGCTGAGATTCTGCAAGCCGTCCCCTCCGGCGAAGGCGAT

Tyros #27

H H A F V D S I F E Q W L Q R H R P L Q E V Y P E A N A P I CACCATGCCTTTGTGGATAGCATTTTCGAACAGTGGCTGCAAAGGCCTTCGCAAGAGGTTTACCCTGAGGCTTACCCTGAGGCTTACCCTGAGGCTTACCCTGATT

TRP-1 #4

CTDDLMGSRSNFDSTLISPNSVPSQWRVVCTGCACAGACGACCAGACGACCAGACGACTCTCTCCCAGTGGAGGGTCCTGTTGACTCCCCCCAATAGCGTCTTCTCCCCAGTGGAGGGTCCTGTGT

MUC1R #18

MUC1R #21

S Y T N P A V A A A S A N L A A AGCTATACCAATCCCGCTGGCTGCCGCTAGCGCTAACCTCGCCGCT

MC1R #19

E H P T C G C I F K N F N L F L A L I I C N A I I D P L I Y GAGCATCCCACATGCGATGCATTTCAAAAACTTTAACCTCTTCCTCGCCCTCATCTATTTGCAATGCCATTATCGATCCCTCATCTAT

Tyros #26

MSQVQGSANDPIFLLHHAFVDSIFEQWLQR ATGTCCCAGGTCCAGGGAAGCGCTAACGATCCCATTTTCCTCCTGCATCACGCTTTCGTCGACTCCATCTTTGAGCAATGGCTCCAGAGA

TRP2 #22

qp100 #19

LISRALVVTHTYLEPGPVTAQVVLQAAIPL

TRP2 #17

S F A L P Y W N F A T G R N B C D V C T D Q L F G A A R P D

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AGCTTTGCCCTACTGGAATTTCGCTACCGGAAGGAATGAGTGTGACGTCTGCACAGACCAACTGTTTGGCGCTGCCAGACCCGAT

gp100 #:

VIGALLAVGATKVPRNQDWLGVSRQLRTKA GTGATTGGCGCTCTGCCGCGCTCCGAGGCTCAGGATGCCTCGGCGTCGCCTCGCCGCGCAGACAGCCTCAGGACAAAGGCT

gp100 #16

A L D G G N K H P L R N Q P L T F A L Q L H D P S G Y L A E GCCCTCGACGGAGGCAATAAGCATTCCTCAGGAATCAGCCTCTGACATTCGCTCTGCAACTGCATGACCTTGACGTACCGCAAACTGACCTTGACGATACCTCGCCGAA

TRP2 #18

C D V C T D Q L F G A A R P D D P T L I S R N S R F S S W E TGCGATGTGTGTCCGGTCCTCGGGAGCCCCTAGGCCTGACGATCCCACACTGATTAGCAGAAACTCCAGGTTTAGCTCCTGGGAA

MART #

A A M P R B D A H P I Y G Y P K K G H G H S Y T T A B B A A GCCGCTATGCCTAGGGAAGACGCTCACTTTATCTATGGCTATCCCAAAAAGGGACACTCCTACACAACCGCTGAGGAAGCCGCT

TRP-1 #11

MUCLR #14

S D V S V S D V P F P F S A Q S G A G V P G W G I A L L V L AGCGATGTCCGTGCTCCCTTTTCCCTTTTAGCGCTCAGTCCGGGGGCTCGCGGTCCCCGGATGGGGATCGCTCTGCTCGTGCTC

TRP2 #10

SPQERBQFLGALDLAKKRVHPDYVITTQHW AGCCCTCAGGAAAGGGAACAGTTTCTGGGAGCCCTCGACCTCGCCAAAAAGAGAGTGCATCCCGATTACGTCATCACAACCCAACACTGG

Tyros #10

F F A Y L T L A K H T I S S D Y V I P I G T Y G Q M K N G S TTCTTTGCCTATCTGACCACTGGCTAAGCATACCATTAGCTCCGACTATGTGATTCCCATTGGCACATACGGACAGATGAAGAATGGCTCC

MC1R #7

G T N V L B T A V I L L B A G A L V A R A A V L Q Q L D N
GGCACAAACGTCCTGGAAACCGCTGTGATTCTGCTCCTGGAAGCCGGAGCCCTCGTGGCTTAGGGCTGCCGTCCTGCAACAGCTCGACAAT

MUC1R #16

MART #6

C P Q B G P D H R D S K V S L Q B K N C E P V V P N A P P A TGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAGTGTCCCTGCAAGAGAAAACTGTGAGCCTGTGGTCCCCAATGCCCCTCCCGCT

MUC1F #5

TRP2 #28

MC1R #21

A F H S Q E L R R T L K E V L T C S W A A GCCTTTCACTCCCAGGAACTGAGAAGGACACTGAAAGAGGTCCTGACATGCTCCTGGGCTGCC

TRP2 #15

FSHQGPAFVTWHRYHLLCLERDLQRLIGNETTCTCCCACCACGACCCTCTTCTCTCGAAAGGCTCTCTCGGAAAGGCTCATCGGAAACGAA

TRP-1 #8

RPMVQRLPEPQDVAQCLEVGLPDTPPPYSNAGGCCTATGGTCCAGAGACTGCTGTTTGACACACCCCCTTTCTATAGCAAT

TRP-1 #13

Q D P I F V L L H T F T D A V F D E W L R R Y N A D I S T F CAGGATCCCATTTTCGTCCTCCTCACACACTTCACAGACGCTGTGTTTGACGAATGGCTCAGGAGATACAATGCCGATATCTCCACCTTT

TRP2 #4

L G A E S A N V C G S Q Q G R G Q C T E V R A D T R P W S G

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CTGGGAGCCGAAAGCGCTAACGTCTGCGGAAGCCAACAGGGAAGGGGACAGTGTACCGAAGTGAGAGCCGATACCAGACCCTGGAGCGGA

TRP2 #8

TRP-1 #12

H L F L N G T G G Q T H L S S Q D P I F V L L H T F T D A V CACCTCTTCCTCAACGGAACCCGAACCCCAACCCCATCTGTCCAGCCAAGACCCTATCTTTGTGCTCCTGCATACCTTTACCGATGCCGTC

Tyros #34

G L V S L L C R H K R K Q L P B B K Q P L L M B K B D Y H S GGCCTCGTGTCCCTGAGAGACACAAAAGGAAACAGCTCCCCGAAGAGAAAACAGCCTCTGCTCATGGAAAAGGAAAAGGAACTATCACTCC

TRP2 #

G C K I L P G A Q G Q P P R V C M T V D S L V N K B C C P R GGCTGTAAGATTCTGCCTGGGGCTCAGGGAATGCTGTCCCAGA

gp100 #43

Q L P H S S S H N L R L P R I P C S C P I G B N S P L L S G CAGCTCCCCCATAGCTCCAGCCATTGGCTCAGCGCTCCCCAGAATCTTTTGCTCCTGCCCTATCGGAGAGAATAGCCCTCTGCTCAGCGGA

gp100 #10

D G G P C P S G S W S Q K R S F V Y V W K T W G Q Y W Q V L GACGGAGGCCCTTGCCCTAGCGGAAGCTGGAGCCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGACAGTATTGGCAAGTGCTC

gp100 #3

N Q D W L G V S R Q L R T K A W N R Q L Y P B W T B A Q R L AACCAAGACTGGCTGGGGGGCTGGGGAGCCCAAAGGCTC

Tyros #14

I W R D I D F A H E A P A F L P W H R L F L L R W B Q E I Q
ATCTGGAGGGATATCGTTTCGCTCACGAAGCCCCTGCCTTTCTGCCTTGGCATAGGCTCTTCCTCCTGAGATGGGAACACGAAATCCAA

MUC1F #1

A A M T P G T Q S P F P L L L L T V L T V V T G S G H A S GCCGCTATGACACCCGGAAGCCCTTCTTTCTGCTCCTGCTCCTGACAGTGCTCACCGTGACAGGCTCCGGCCATGCCTCC

MART #5

D K S L H V G T Q C A L T R R C P Q E G F D H R D S K V S L GACAAAAGCCTCCACGTCGGCACACAGTGTGCCCTCACCAGAAGGTGTCCCCAAGAGGGTTCGATCACAGAGACTCCAAGGTCAGCCTC

MUCIR #2

Tyros #24

L B G F A S F L T G I A D A S Q S S M H N A L H I Y M N G T CTGGAAGGCTTTGCCTCCCCCCTCACCGGAATCGCTGACGCTAGCCAAGCTCCATGCATAACGCTCTGCATATCTATATGAATGGCACA

TRP2 #14

R D T L L G P G R P Y R A Y D F S H Q G P A F V T W H R Y H AGGGATACCTCCTGGGACCCGGAAGGCCTTACAGAGCCATTGACTTTAGCCATCAGGGACCCGCTTTCGTCACCTGGCACAGATACCAT

Tyros #1

A A M L L A V L Y C L L W S F Q T S A G H F P R A C V S S K GCCGCTATGCTCCTGGCTGTGCTCTGGTCCTGCCCGGACACTTTCCCAGAGCCTGTGTGTCCAGAAA

gp100 #35

A F E L T V S C Q G G L P K E A C M E I S S P G C Q P P A Q GCCTTTGAGCTCACCGTCAGCTCAGGGAGGCCTCCCCAAAGAGGCTTGCATGGAGATTAGCTCCCCGGATGCCAACCCCCTGCCCAA

Tyros #6

V D D R B S W P S V F Y N R T C Q C S G N F M G F N C G N C GTGGATGACAGAGAGTCCTGGCCTAGCGTCTTCTATAACAGAACCTGTCAGTGTAGCGGAAACTTTATGGGATTCAATTGCGGAAACTGT

qp100 #34

ESAEILQAVPSGEGDAFELTVSCQGGLPKEGAGTCCCCAAGCCGGACTGCCTAAGGAA

TRP2 #20

T V C D S L D D Y N H L V T L C N G T Y E G L L R R N Q M G

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ACCOTCTGCGATAGCCTCGACGATTACAATCACCTCGTGACACTGTGTAACGGAACCTTATGAGGGACTGCTCAGGAGAAACCAAATGGGA

Tyros #5

L L S N A P L G P Q F P F T G V D D R B S W P S V F Y N R T CTGCTCAGCAATGCCCCTCTGGGACCCCAATTCCCTTTCACAGGGCTCGACGATAGGGAAAGCTGGCCCTCCGTGTTTTACAATAGGACA

MART #8

Y B K L S A B Q S P P P Y S P A A TACGAAAAGCTCAGCGCTGAGCAAAGCCCTCCCCCTTACTCCCCCGCTGCC

gp100 #41

IVGILLVLMAVVLASLIYRRRLMKQDFSVPATCGTCGCTTCGTCCTCGTCCTCATCTATAGGAGAAGGCTCATGAAACAGGATTTCTCCGTGCCT

MART H

Tyros #31

YSYLQDSDPDSPQDYIKSYLBQASRIWSWLTACTCCTACCTCCAGGATACCGATCCCGATAGCTTTCAGGATTACATTAAGTCCTACCTCCGAGCAAGCCTCCAGGATTTGGTCCTGGCTC

MUC1F #6

Q G Q D V T L A P A T B P A S G S A A T W G Q D V T S V P V CAGGGACAGGATGTGACACTGGCTACCGGAACCCGCTAGCGGAAGCGCTGCCACATGGGGACAGGATGTGACAAGCGTCCCCGTC

gp100 #21

T S C G S S P V P G T T D G H R P T A B A P N T T A G Q V P ACCTCCTGCGGAAGCTCCCCGGGAACCACAGACGGACCACAGCCGAAGCCCCTAACACACCGCTGGCCAAGTGCCT

MUCIR #3

TRP2 #32

E E T P G W P T T L L V V M G T L V A L V G L P V L L A P L GAGGAAACCCTGGCGCACAACCCTCGTGGTCGGCACACCGTTGGCCCTGGGGACTGTTTGTGCTCCTGGCTTTTCCTC

gp100 #29

T T T E N V E T T A R E L P I P E P E G P D A S S I M S T E ACCACAACCGAATGGGTCGAGACCGCTAGGGAACTGCCTTATCCCTGAGGCTCGAGGACCCGATGCCTCCAGCATTATGTCCACCGAA

MC1R #17

Tyros #33

L G A A M V G A V L T A L L A G L V S L L C R H K R K Q L P CTGGGAGCCGCTATGGTCGGCGCTCTCGCCGGCTCTGCTCGCCGGCTCTGTTAGGCATAGAGAAAGCAACTGCCT

MC1R #8

G A L V A R A A V L Q Q L D N V I D V I T C S S M L S S L C GGCGCTCTGGTCGCCAGGAGCCGCTGCTCCAGCAACTGGATAACGTCATCGATGTGATTACCTGTAGCTCCATGCTCAGCTCCCTGTGT

mp100 #26

M T P B K V P V S B V M G T T L A B M S T P B A T G M T P A ATGACACCCGAAAAGGTCCCCGTCAGCGAAGTGACACCCCCCGAAATGTCCACCCCTGAGGCTACCGGAATGACACCCCCCT

Tyros #2

MC1R #11

A L R Y H S I V T L P R A P R A V A A I W V A S V V F S T L GCCCTCAGGTATCACTCCACCCTCCCCAGAGCCCCTAGGGCTGCCATTTGGGTGCCTCCCCTGGTCTTCTCCACCCTC

MUCIR #12

FREGTINVHDVETQFNQYKTEAASRYNLTI TTCAGAGAGGGAACCATTAACGTCCACGATGTGGAAACCCAATTCAATCAGTATAAGACAGAGGCTGCCTCCAGGTATAACCTCACCATT

Tyros #3

N L M B K B C C P P W S G D R S P C G Q L S G R G S C Q N I

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AACCTCATGGAAAAGGAATGCTGTCCCCCTTGGTCCGGCGATAGGTCCCCCTGTGGCCAACTGTCCGGCAGAGGCTCCTGCCAAAACATT

Tyros #32

IKSYLBQASRIWSWLLGAAMVGAVLTALLAATCAAAAGCTATCTGGAACAGCCTACGGGGCTGCCATGGTGGGAACCGGCCTCCTGGGCTGCCATGGTGGGAGCCGTCCTGACAGCCCTCCTGGCT

MUC1R #5

MICIR #15

S G A G V P G W G I A L L V L V C V L V A L A I V Y L I A L AGGGGAGGCGGAGTGCCTGGGGATTGCCCTCCTGGTCCTGGTCTGGTCTGGTCTGGTCCTGGTCCTCGCCCATTGTGTATCTGATTGCCCTC

MC1R #10

FLGAIAVDRYISIFYALRYHSIVTLPRAPRTTCCTCGGCGCTATCGCTATGGCATAGCATTGTGACACTGCCTAGGGCTCCCAGA

gp100 #40

LIMPGQEAGLGQVPLIVGILLVLMAVVLAS

TRP2 #3

T L V A L V G L F V L L A F L Q Y R R L R K G Y T P L M B T ACCCTCGTGGCTCTGGTCGGCCTCTTCGTCCTGCTCGCCTTTCTGCAATACAGAAGGCTCAGGAAAGGCTATACCCCTCTGATGGAGACA

TRP-1 #5

L I S P N S V F S Q W R V V C D S L B D Y D T L G T L C N S CTGATTAGCCCTAACTCCGTGTTTAGCCAATGGAGAGTGGTCTGCGATAGCCTCGAGGATTACCGTGACACACTGTGTAACTCC

MCIP #2

L N S T P T A I P Q L G L A A N Q T G A R C L E V S I S D G CTGAATAGCACCCCACAGCCATTCCCCAACTGGGACTGCCCAACTGGCATCAGACAGGCGCTTAGGTGTCTTGGAAGTGTCCATCTCCGACGGA

Tyros #28

HRPLQEVYPEANAPIGHNRESYMVPFIPLY

gp100 #24

TRP2 #11

K K R V H P D Y V I T T Q H W L G L L G P N G T Q P Q F A N AAGAAAAGGGTCCACCCTGACTATGGATTACCACACGCATGGCTCCTGGGACCCAATGGCACAGCCTCAGTTTGCCAAT

gp100 #38

LHQILKGGSGTYCLNVSLADTNSLAVVSTQ

qp100 #30

P B P B G P D A S S I M S T B S I T G S L G P L L D G T A T CCCGAACCCGAAGGCCCTGACGCTAGCTCCATCATGAGCACAGAGTCCATCACAGGCTCCCTGGGACCCCTCCTGGATGGCACAGCCACA

gp100 #31

S I T G S L G P L L D G T A T L R L V K R Q V P L D C V L Y
AGCATTACCGGAAGCCTCGGCCCTCTGCTCGACCGTACCCTCAGGCTCGTGAAAAGGCAAGTGCCTCTGGATTGCGTCCTGTAT

00100 #5

D C W R G G Q V S L K V S N D G P T L I G A N A S F S I A L GACTGTTGGAGAGGCGGACAGGTCAGCTCAAGGTCAGCAATGACGGACCCACACTGATTGGCGCTAACGCTAGCTTTAGCATTGCCCTC

Synthetic Protein:

WHRQLYPEWTBAQRLDCWRGGQVSLKVSNDPYILRNQDDRELWPRKFPHRTCKCTGNFAGRNGDFFISSKDLGYDYSYLQDSDPDSPQDYAAPAFLTW
HRYHLLRLBKDMQBMLQBPSFSGHNRESYMVPFIPLYRNGDFFISSKDLGYDLLCLERDLQRLIGNESFALPYWNFATGRNETTEVVGTTPGQAPTAB
PSGTTSVQVPTTEVSTDYYQBLQRDISEMFLQIYKQGGFLGLSNACMBISSFGCQPPAQRLCQPVLPSPACQLVDQLGYSYAIDLPVSVEETPGWPTT
LLVVMGTEDGPIRRNFAGNVARPMVQRLPBPQDVAQCMTVDSLVNKECCFPLGABSANVCGSQQGRNQYKTRAASRYNLTISDVSVSDVPPPFSAQAA
MSPLWWGFLLSCLGCKILPGAQGQFPRVADLSYTWDFGDSSGTLISRALVVTHTYLBPLAEMSTPEATGMTPAEVSIVVLSGTTAAQVIKPRPGSVVV
QLTLAFREGTINVHDVETQFGSAATMGQDVTSVPVTRPALGSTTPPAHDVLHKRQRPWPQGFGLKGAVTLTILLGIFFLCLALIICNAIIDPLIYAFH
SQBLRRTLKEVLKFFHRTCKCTGNFAGYNCGDCKFGWTGPNCLSLQKFDNPPFFQNSTFSFRNALEGFDKADSKSTPPSIPSHHSDTPTTLASHSTKT
DASSAANRPALGSTAPPVHNVTSASGSASGSASTCNGTYEGLLRRNQMGRNSMKLPTLKDIRDCTHHSSVPPLTSSNHSTSPQLSTGVSPPFLSFIAY

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YDHVAVLLCLVVFFLAMLVLMAVLYVKLTGDENFTI PYWDWRDAEKCDI CTDEYMGLRLVKRQVPLDCVLYRYGSFSVTLDI VQGI FLQI YKQGGFLG LSNIKPRPGSVVVQLTLAVIDVITCSSMLSSLCFLGA1AVDRYISIFYRNPGNHDKSRTPRLPSSADVEFCLSLTQYEFDEWLRRYNADISTFPLENA PIGHNRQYNMVSLADTNSLAVVSTQLIMPGQEAGLGQVPLGPVTAQVVLQAAIPLTSCGSSPVPGTTDGHKPGFWGPNCTERRLLVRRNIFDLSAPEK DKLGTHTMEVTVYHRRGSRSYVPLAHSSSAFTAVAAIWVASVVFSTLFIAYYDHVAVLLCLVGTLDSQVMSLHNLVHSFLNGTNALPHSAANGCMYCR rrngyralmdkslhvgtqcaltrrpwhrlfllrweqbiqkltgdenfti pywdwaamavqgsqrrllgslnstptaipqlglaavvatiaknrnlhsp MYCPICCLALSDLLVSQSSMHNALHIYMNGTMSQVQGSANDPIPLLGQHPTNPNLLSPASPFSSWQIVCSRLEEYNYCPICCLALSDLLVSGTNVLBT AVILLLEADPTLISRNSRPSSWETVCDSLDDYNHLVTLTRPALGSTTPPAHDVTSAPDNKAARDAEKCDICTDEYMGGQHPTNPNLLSPASPTFALQL hdpsgylaeadlsytwdfgdssgtssadvefclsltqyesgsmdkaanpsfrntgptliganasfsialnppgsqkvlpdgqviwgpfflhltlivic PEHPTCGCIFKNFNLFCQCSGNFMGFNCGNCKFGFWGPNCTERRLLQYRRLRKGYTPLMETHLSSKRYTEEAAAPLENAPIGHNRQYNMVPFWPPVTN temfvtnppgsqkvlpdgqviwvnntiingsqvwggrptaeapnttagqvpttevvgttpgqaptastpggeketsatqrssvpssteknavsmtsli ${\tt YRRRLMKQDFSVPQLPHSSSHWLRLPRILGLLGPNGTQPQFANCSVYDFFVWLHYYSVCLEVGLFDTPPFYSNSTNSFRNTVEGYSDPAAMDLVLIRC$ llhlavigallavgatkvprnqtgarclevsisdglplslglvslvenalsgsmdkaanfsfrntlegfaspltgiadasspcgqlsgrgscqnills NAPLGPQFPFTGMHYYVSMDALLGGSBINRDIDFAHEAPAFLEEKQPLLMEKEDYHSLYQSHLAAGQCTEVRADTRPWSGPYILRNQDDRELWPRSVP SSTEKNAVSMTSSVLSSHSPGSGSSTTTPMFNDINIYDLFVWMHYYVSMDALLGGSEQPVYPQETDDACIFPDGGPCPSGSWSQKRSDSLKDYDTLGT LCNSTEDGPIRRNPAGNVAWVNNTIINGSQVWGGQPVYPQETDDACIFPQEKNCEPVVPNAPPAYEKLSAEQSPPPYSPSRSYVPLAHSSSAFTITDQ vppsvsvsqlrlekdmqemlqepspslpymnpatgknvcdivpfwppvtnytemfvtapdnlgytybaacsvydffvwlhyysvrdtligpgrpyraid vrrnifdlsapekdkppayltlakhtissdkkghghsyttabbaagigiltvilgvlllifvyvwkthgqynqvlggpvsglsigtgramggpvsgls IGTGRAMLGTHTMEVTVYHRRGISTAPVQMPTAESTGMTPEKVPVSEVMGTTFSSWQIVCSRLEEYNSHQSLCNGTPEGPLRDPIFVVLHSFTDAIFD EWMKRFNPPADAWPHMLARACQHAQGIARLHKRQRPVHQGFGLKLLTVLTVVTGSGHASSTPGGEKETSATQRSFCSCPIGENSPLLSGOOVAATPSF RNALEGFDKADGTLDSQVMSLHNLVHSHQSLCNGTPEGPLRRNPGNHDKSRTPRLPPFFPPVTNEELFLTSDQLGYSYAIDLPVSVERKKPPVIRQNI hslspqereqplgaldlaqblapighnrwynmvpppppvtneelpltsbvsivvlsgttaaqvtttbwvbttarblpitspqlstgvsppplsphisn lopnssledpyhthgryvppsstdrspyekvsagnggssllflslglvslvenalvvatiaknrnlhspmsflngtnalphsaandpipvvlhsptda IFAVCQCRRKNYGQLDIFPARDTYHPMSEYPTVFFLAMLVLMAVLYVHMLARACQHAQGIARSTNSFRNTVEGYSDPTGKYDPAVRSLHNLALPYKNF ${\tt ATGKNVCDICTDDL{\tt MGSRSNPDSTITDQVPFSVSVSQLRALDGGNKHFLRNQPLFHISNLQFNSSLEDPSTDYYQBLQRDISEMSPYEKVSAGNGGSS$ LSYTNPAVAAASANLAYVI PIGTYGQMKNGSTPMFNDINIYDLFVWRLCQPVLPSPACQLVLHQILKGGSGTYCLNRYGSFSVTLDIVQGIESABILQ avpsgegdhhafvdsifeqwlqrhrplqevypeanapictddlmgersnpdstlispnsvfsqwrvvcfpardtyhpmsbyptyhthgryvppsstdr SYTNPAVAAASANLAABHPTCGCIPKNFNLPLALIICNAIIDPLIYMSQVQGSANDPIPLLHHAFVDSIFEQWLQRRNSMKLPTLKDIRDCLSLQKFD nppppqnslisralvvthtylbpgpvtaqvvlqaaiplsfalpywnpatgrnecdvctdqlfgaarpdvigallavgatkvprnqdwlgvsrqlrtka ALDGGNKHPLRNOPLTPALQLHDPSGYLAECDVCTDQLPGAARPDDPTLISRNSRFSSWEAAMPREDAHFIYGYPKKGHGHSYTTAERAATGKYDPAV RSLHNLAHLFINGTGGQTHLSSSDVSVSDVPPPPSAQSGAGVPGWGIALLVLSPQEREQFLGALDLAKKRVHPDYVITTQHWPFAYLTLAKHTISSDY vipigtygqmkngsgtnvlbtavillleagalvaraavlqqldnvcvlvalaivylialavcqcrknygqldicpqbgpdhrdskvslqbkncbpvv PNAPPASVLSSHSPGSGSSTTQGQDVTLAPATEPASDEWMKRFNPPADAWPQELAPIGHNRMYNMVAFHSQELRRTLKEVLTCSWAAFSHQGPAFVTW HRYHLLCLERDLQRLIGNERPMVQRLPEPQDVAQCLEVGLFDTPPPYSNQDPIFVLLHTFTDAVFDEWLRRYNADISTFLGAESANVCGSQQGRGQCT evradtrpwsgyncgdckfgwtgpncerkkppvirqnihslhlflwgtggqthlssqdpifvllhtftdavglvsllcrhkrkqlpeekqpllweked YHSGCKILPGAQGQPPRVCMTVDSLVNKBCCPRQLPHSSSHWLRLPRIPCSCPIGENSPLLSGDGGPCPSGSWSQKRSFVYVWKTWGQYWQVLNQDWL GVSRQLRTKAWNRQLYPEWTEAQRLIWRDIDPAHEAPAPLPWHRLFLLRWEQBIQAAMTPGTQSPFFLLLLLTVITVVTGSGHASDKSLHVGTQCALT rrcpqbcfdhrdskvslnvtsasgsasgsastlvhngtsaratttpalbgfaspltgiadasqssmhnalhiymngtrdtllgpgrpyraidfshqgp AFVTWHRYHAAMLLAVLYCLLWSFQTSAGHFPRACVSSKAFBLTVSCQGGLPKEACMBISSPGCQPPAQVDDRESWPSVFYNRTCQCSGNFMGFNGGN CESABILQAVPSGEGDAPELTVSCQGGLPKETVCDSLDDYNHLVTLCNGTYEGLLRNQMGLLSNAPLGPQFPFTGVDDRESWPSVFYNRTYEKLSAE QSPPPYSPAAIVGILLVLMAVVLASLIYRRRLMKQDFSVPGIGILTVILGVLLLIGCWYCRRRNGYRALMYSYLQDSDPDSPQDYIKSYLEQASRIWS wlqqqdvtlapatepasgsaatwqqdvtsvpvtscgsspvpgttdghrptaeapnttacqvplvhngtsaratttpaskstpfsipshhsdteetpgw PTTLLVVMGTLVALVGLFVLLAFLTTTEMVETTARELPIPEPEGPDASSIMSTEGAVTLTILLGIFFLCWGPFFLHLTLIVLCPLGAAMVGAVLTALL aglvsllcrhkrkqlpgalvaraavlqqldnvidvitcssmlsslchtpbkvpvsbvmgttlaemstpbatgmtpaqtsaghppracvssknlmbkec CPPWSGDRALRYHSIVTLPRAPRAVAAIWVASVVFSTLFREGTINVHDVETQFNQYKTEAASRYNLTINLMEKECCPPWSGDRSPCGQLSGRGSCQNI iksyleqasriwswligaamvgavltallapttlashstktdassthhssvppltssnhssgagvpgwgiallvlvcvlvalaivylialpigaiavd RYISIFYALRYHSIVTLPRAPRLIMPGQEAGLGQVPLIVGILLVLMAVVLASTLVALVGLFVLLAFLQYRRLRKGYTPLMETLISPNSVFSQMRVVCD Sledydtlgtlcnsinstptaipqlglaanqtgarclevsisdghrplqevypeanapighnresymvppiplyepsgttsvqvpttevistapvqnp taestgkkrvhpdyvittqhnigligpngtqpqpanlhqilkggsgtyclnvsladtnslavvstqpepegpdassimstesitgsigpllogtatsi TGSLGPLLDGTATLRLVKRQVPLDCVLYDCWRGGQVSLKVSNDGPTLIGANASFSIAL

Synthetic DNA:

TGGAATAGGCAACTGTATCCCGAATGGACAGAGGGTCAGAGACTGGATTGCTGGAGGGGAGGCCAAGTGTCCCTGAAAGTGTCCCAACGATCCCTATAT TTATCTCCAGCAAAGACCTCGGCTATGACTATAGCTATCTGCAAGACTCCGACCCTGACCTCTTCCAAGACTATGCCGCTCCCGCTTTCCTCACCTGG ${\tt CACAGATACCATCTGCTCAGGCTCGAGAAAGACATGCAGGAAATGCTCCAGGAACCCTCCTTCTCCGGCCATAACAGAGAGTCCTACATGGTGCCTTT$ ATGAGTCCTTCGCTCTGCCTTACTGGAACTTTGCCACAGGCAGAAACGAAACCACAGAGGTCGTGGGAACCACACCCGGACAGGCTCCCACAGCCGAA $\tt CTATAAGCAAGGCGGATTCCTCGGCCTCAGCAATGCCTGTATGGAAATCTCCAGCCCTGGCTGTCAGCCTCCCGCTCAGAGACTGTGTCAGCCTGTGC$ TCCCCTCCCCGCTTGCCAACTGGTCGACCAACTGGGATACTCCTACGCTATCGATCTGCCTGTGTCCGTGGAAGAGACACCCGGATGGCCTACCACA CTGCTCGTGGTCATGGGAACCGAAGACGGACCCATTAGGAGAAACCCTGCCGGAAACGTCGCCAGGACCCATGGTGCAAAGGCTCCCCGAACCCCAAGA GAAACCAATACAAAACCGAAGCCGCTAGCAGATACAATCTGACAATCTCCGACGTCAGCGTCAGCGATGTGCCTTTCCCCTTTCTCCGCCCAAGCCGCT ATGTCCCCCCTCTGGTGGGGCTTTCTGCTCAGCTGTCTGGGATGCAAAATCCTCCCGGAGCCCAAGGCCAATTCCCTAGGGTCGCCGATCTGTCCTA AAGCCACAGGCATGACCCCTGCCGAAGTGTCCATCGTCGTGCTCAGCGGAACCACAGCCGCTCAGGTCATCAAATTCAGACCCCGGAAGCGTCGTGGTC CAGCTCACCTCGCCTTTAGGGAAGGCACAATCAATGTGCATGACGTCGAGACACAGTTTGGCTCCGCCGCTACCTGGGGCCAAGACGTCACCTCCGT GCCTGTGACAAGGCCTGCCCTCGGCTCCACCACCCCCTGCCCATGACGTCCTGCATAAGAGACAGAGACCCGTCCACCAAGGCTTTGGCCTCAAGG AGCCAAGAGCTCAGGAGAACCCTCAAGGAAGTGCTCAAGTTTTTCCATAGGACATGCAAATGCACAGGCAATTTCGCTGGCTATAACTGTGGCGATTG

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GACGCTAGCTCCGCCGCTAACAGACCCGCTCTGGGAAGCACAGCCCCTCCCGTCCACAATGTGACAAGCGCTAGCGGAAGCGCTAGCGGAAGCGCTAG TACGATCACGTCGCCGTCCTGCTCTGCTCTTCTTCTTCTGGCTATGCTCATGGCTGTGCTCTACGTCAAGCTCACCGGAGACGAAAA TCGACTGTGTGCTCTACAGATACGGAAGCTTTAGCGTCACCCTCGACATTGTGCAAGGCATTTTCCTCCAGATTTACAAACAGGGAGGCTTTCTGGGA CTGTCCAACATTAAGTTTAGGCCTGGCTCCGTGGTCGTGCAACTGACACTGGCTGTGATTGACGTCATCACATGCTCCAGCATGCTGTCCAGCCTGTG CTTTCTGGGAGCCATTGCCGTCGACAGATACATTAGCATTTTCTATAGGAATCCCGGAAACCATGACAAAAGCAGAACCCCTAGGCTCCCCTCCAGCG CTGACGTCGAGTTTTGCCTCAGCCTCACCCAATACGAATTCGATGAGTGGCTGAGAAGGTATAACGCTGACATTAGCACATTCCCTCTGGAAAACGCT CCCATTGGCCATAACAGACAGTATAACATGGTGTCCCTGGCTGACACAAACTCCCTGGCTGTGGTCAGCACACAGCTCATCATGCCCGGACAGGAAGC CGGACTGGGACAGGTCCCCCTCGGGCCCTGTGACAGCCCAAGTGGTCCTGCAAGCCGCTATCCCTCTGACAAGCTGTGGCTCCAGCCCTGTGCCTGGCA GACAAACTGGGAACCCATACCATGGAGGTCACCGTCTACCATAGGAGAGGCTCCAGGTCCTACGTCCCCCCCATAGCTCCAGCGCTTTCACAGC CGTCGCCGCTATCTGGGTGGCTAGCGTCGTGTTTAGCACACTGTTTATCGCTTACTATGACCATGTGGCTGTCTCCTGTGTCTGGTCGGCACACTGG AGGAGAAACGGATACAGAGCCCTCATGGATAAGTCCCTGCATGTGGGAACCCAATGCGCTCTGACAAGGAGACCCTGGCACAGACTGTTTCTGCTCAG GTGGGAGCAAGAGATTCAGAAACTGACAGGCGATGAGAATTTCACAATCCCTTACTGGGACTGGGCCGCTATGGCTGTGCAAGGCTCCCAGAGAAGGC TCCTGGGAAGCCTCAACTCCACCCCTACCGCTATCCCTCAGCTCGGCCTCGCCGCTGTGGTCGCCACAATCGCTAAGAATAGGAATCTGCATAGCCCT ATGTATTGCTTTATCTGTTGCCTCGCCCTCAGCGATCTGCTCGTGTCCCAGTCCAGCATGCACAATGCCCTCCACATTTACATGAACGGAACCATGAG AAATCGTCTGCTCCAGGCTCGAGGAATACAATTACTGTTTCATTTGCTGTCTGGCTCTGTCCGACCTCCTGGTCAGCGGAACCAATGTGCTCGAGACA GCCGTCATCCTCCTGCTCGAGGCTGACCCTACCCTCATCTCCAGGAATAGCAGATTCTCCAGGTGGGAGACAGTGTGTGACTCCCTGGATGACTATAA CCATCTGGTCACCCTCACCAGACCCGGCTCTGGGAAGCACAACCCCTCCCGCTCACGATGTGACAAGCGGCTCCCGATAACAAAGCCGCTAGGGATGCCG AAAAGTGTGACATTTGCACAGACGAATACATGGGCGGACAGCATCCCACAAACCCTAACCTCCTGTCCCCCGCTAGCTTTACCTTTGCCCTCCAGCTC CACGATCCCTCCGGCTATCTGGCTGAGGCTGACCTCAGCTATACCTGGGACTTTGGCGATAGCTCCGGCACAAGCTCCGCCGATGTGGAATTCTGTCT GTCCCTGACACAGTATGAGTCCGGCTCCATGGATAAGGCTGCCAATTTCTCCTTCAGAAACACAGGCCCTACCCTCATCGGAGCCAATGCCTCCTTCT CCATCGCTCTGAATTTCCCTGGCTCCCAGAAAGTGCTCCCCGATGGCCAAGTGATTTGGGGGACCCTTTTTCCTCCACCTCACCCTCATCGTCCTGTGT CCCGAACACCCTACCTGTGGCTGTATCTTTAAGAATTTCAATCTGTTTTGCCAATGCTCCGGCAATTTCATGGGCTTTAACTGTGGCAATTGCAAATT CGGATTCTGGGGCCCTAACTGTACCGAAAGGAGACTGCTCCAGTATAGGAGACTGAGAAAGGGATACACACCCCTCATGGAAACCCATCTGTCCAGCA AAAGGTATACCGAAGAGGCTGCCGCTCCCCTCGAGAATGCCCCCTATCGGACACAATAGGCAATACGAATATGGTCCCCTTTTGGCCTCCCGTCACCAAT GTGGGGCGGAAGGCCTACCGCTGAGGCTCCCAATACCACAGCCGGACAGGTCCCCACAACCGAAGTGGTCGGCACACCCCTGGCCAAGCCCCTACCG CTAGCACACCCGGAGGGGAAAAGGAAACCTCCGCCACAGAGAGGAGCCTCCGTGCCTAGCTCCACCGAAAAGAATGCCGTCAGCATGACCTCCCTGATT TACAGAAGGAGACTGATGAAGCAAGACTTTAGCGTCCCCCAACTGCCTCCAGCTCCCACTGGCTGAGACTGCCTAGGATTCTGGGACTGCTCGG $\tt CCCTAACGGAACCCCAACTCGCTAACTGTAGCGTCTACGATTTCTTTGTGTGGCTGCATTACTATAGCGTCTGCCTCGAGGTCGGCCTCTTCG$ ATACCCCTCCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCTGCCGCTATGGATCTGGTCCTGAAAAGGTGT CTGCTCCACCTCGCCGTCATCGGAGCCCTCCTGGCTGTGGGAGCCACAAAGGTCCCCAGAAACCAAACCGGAGCCAGATGCCTCGAGGTCAGCATTAG CGATGGCCTCTTCCTCAGCCTCGGCCTCGTGTCCCTGGTCGAGAATGCCCTCAGCGGAAGCATGGACAAAGCCGCTAACTTTAGCTTTAGGAATACCC TCGAGGGATTCGCTAGCCCTCTGACAGGCATTGCCGATGCCTCCAGCCCTTGCGGACAGCTCAGCGGGAAGGCTGTCAGAATATCCTCCTGTCC AACGCTCCCCTCGGCCCTCAGTTTCCCTTTACCGGAATGCATTACTATGTGTCCATGGATGCCCTCCTGGGAGGCTCCGAGATTTGGAGAGACATTGA CTTTGCCCATGAGGCTCCCGCTTTCCTCGAGGAAAAGCAACCCCTCCTGATGGAGAAAGAGGATTACCATAGCCTCTACCAAAGCCATCTGGCTGCCG GCCAATGCACAGAGGTCAGGGCTGACACAAGGCCTTGGTCCGGCCCTTACATTCTGAGAAACCAAGACGATAGGGAACTGTGGCCCAGAAGCGTCCCC TATCAATATCTATGACCTCTTCGTCTGGATGCACTATTACGTCAGCATGGACGCTCTGCTCGGCGGAAGCGGAACAGCCTGTGTATCCCCCAAGAGACAG ACGATGCCTGTATCTTTCCCGATGGCGGACCCTGTCCCTCCGGCTCCTGGTCCCAGAAAAGGTCCGACTCCCTGGAAGACTATGACACACTGGGAACC CTCTGCAATAGCACAGAGGATGGCCCTATCAGAAGGAATCCCGCTGGCAATGTGGCTTGGGTCAACAATACCATTATCAATGGCTCCCAGGTCTGGGG AGGCCAACCCGTCTACCCTCAGGAAACCGATGACGCTTGCATTTTCCCTCAGGAAAAGAATTGCGAACCCGTCGTGCCTAACGCTCCCCCTGCCTATG AGAAACTGTCCGCCGAACAGTCCCCCCCCCCCCTATAGCCCTAGCAGAAGCTATGTGCCTCTGGCTCACTCCAGCTCCGCCTTTACCATTACCGATCAG GTCCCCTTTAGCGTCAGCGTCAGCCCAACTGAGACTGGAAAAGGATATGCAAGAGATGCTGCAAGAGCCTAGCTTTAGCCTCCCCTATTGGAATTTCGC ${\tt AGGCTGCCTGGTGTGTGTGTCTGGCTCCACTATTACTCCGTGAGAGACACACTGCTCGGCCGGGCAGACCCTATAGGGCTATCGAT}$ GTGAGAAGGAATATCTTTGACCTCAGCGCTCCCGAAAAGGATAAGTTTTTCGCTTACCTCACCCTCGCCAAACACACAATCTCCAGCGATAAGAAAGG AAACCTGGGGCCAATACTGGCAGGTCCTGGGAGGCCCTGTGTCCGGCCTCAGCATTGGCACAGGGCAGAGCCATGGGCGACCCGTCAGCGGACTGTCC ATCGGAACCGGAAGGGCTATGCTCGGCACACACACAATGGAAGTGACAGTGTATCACAGAAGGGGGAATCTCCACCGCTCCCGTCCAGATGCCCACAGC ATAACTCCCACCAAAGCCTCTGCAATGGCACACCCGAAGGCCCTCTGAGAGACCCTATCTTTGTGGTCCTGCATAGCTTTACCGATGCCATTTTCGAT GAGTGGATGAAAAGGTTTAACCCTCCCGCTGACGCTTGGCCTCACATGCTGGCTAGGGCTTGCCAACACGCTCAGGGAATCGCTAGGCTCCACAAAAG GCAAAGGCCTGTGCATCAGGGATTCGGACTGAAACTGCTCACCGTCCTGACAGTGGTCACCGGAAGCGGACACGCTAGCTCCACCCCTGGCGGAGAGA ${\tt AAGAGACAAGCGCTACCCAAAAGGTCCTTCTGTAGCTGTCCCATTGGCGAAAACTCCCCCCTCCTGTCCGGCCAACAGGTCGCCGCTACCTTTAGCTTT$ AGGANTECCCTCGAGGGATTCGATAAGGCTGACGGAACCCTCGACTCCCAGGTCATGTCCCTGCATAACCTCGTGCATAGCCATCAGTCCCTGTGTAA AACTGTTTCTGACAAGCGATCAGCTCGGCTATAGCTATGCCATTGACCTCCCCGTCAGCGTCGAGAGAAAACCAAAACCCCCTGTGATTAGGCAAAACATT CACTCCCTGTCCCCCAAGAGAGAGAGAGCAATTCCTCGGCGCTCTGGATCTGGCTCAGGAACTGGCTCCCATTGGCCATAACAGAATGTATAACATGGT GCCTTTCTTTCCCCCTGTGACAAACGAAGAGCTCTTCCTCACCTCCGAGGTCAGCATTGTGGTCCTGTCCGGCACAACCGCTGCCCAAGTGACAACCA ${\tt CAGAGTGGGTAAACCACAGGCCAGAGAGCTCCCCATTACCTCCCCCCAACTGTCCACCGGAGTGTCCTTCTTTTTCCTCAGCTTTCACATTAGCAAT}$ $\tt CTGCAATTCAATAGCTCCCTGGAAGACCCTTACCATACCCATGGCAGATACGTCCCCCTAGCTCCACCGATAGGTCCCCCTATGAGAAAGTGTCCGC$ CGGAAACGGAGGCTCCAGCCTCCTGTTTCTGTCCCTGGGACTGGTCAGCCTCGTGGAAAACGCTCTGGTCGTGGCTACCATTGCCAAAAACAGAAACCTCCACTCCCCATGAGCTTTCTGAATGGCACAAACGCTCTGCCTCACTCCGCCGCTAACGATCCCATTTTCGTCGTGCTCCACTCCTTCACAGACGCT ATCTTTGCCGTCTGCCAATGCAGAAGGAAAAACTATGGCCAACTGGATATCTTTCCCGCTAGGGATACCTATCACCCTATGTCCGAGTATCCCACAGT GTTTTTCCTCGCCATGCTGGTCCTGATGGCCGTCCTGTATGTGCATATGCTCGCCAGAGCCCTGTCAGCATGCCCAAGGCATTGCCAGAAGCACAAACT

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 ${\tt CCTTCAGAAACACAGTGGAAGGCTATAGCGATCCCACAGGCAAATACGATCCCGCTGTGAGAAGCCTCCACAATCTGGCTCTGCCTTACTGGAACTTT}$ GCCACAGGCAAAAACGTCTGCGGATATCTGTACCGATGACCTCATGGGAAGCAGAAGCAATTTCGATAGCACAATCACAGACCAAGTGCCTTTCTCCGT GTCCGTGTCCCAGCTCAGGGCTCTGGATGGCGGAAACAACCCAACCTTTCTGAGAAACCACCCCTCTTCCATATCTCCAACCTCCAGGTTTAACTCCAGCC CTGTCCTACACAAACCCTGCCGTCGCCGCCGCCCCAATCTGGCTTACGTCATCCCTATCGGAACCTATGGCCAAATGAAAAACGGAAGCACACC TCAAGGGAGGCTCCGGCACATACTGTCTGAATAGGTATGGCTCCTTCTCCGTGACACTGGATATCGTCCAGGGAATCGAAAGCGCTGAGATTCTGCAA GGCTAACGCTCCCATTTGCACAGACGATCTGATGGGCTCCAGGTCCAACTTTGACTCCACCCTCATCTCCCCCAATAGCGTCTTCTCCCAGTGGAGGG CCTCATCATTTGCAATGCCATTATCGATCCCCTCATCTATATGTCCCAGGTCCAGGGAAGCGCTAACGATCCCATTTTCCTCCTGCATCACGCTTTCG TCGACTCCATCTTTGAGCAATGGCTCCAGAGAAGGAATAGCATGAAGCTCCCCACACTGAAAGACATTAGGGATTGCCTCAGCCTCCAGAAATTCGAT AACCCTCCCTTTTTCCAAAACTCCCTGATTAGCAGAGCCCTCGTGGTCACCCATACCTATCTGGAACCCGGACCCGTCACCGCTCAGGTCGTGCTCCA GACCCGATGTGATTGGCGCTCTGCTCGCCGTCGGCGCTACCAAAGTGCCTAGGAATCAGGATTGGCTCGGCGTCAGCAGACAGCTCAGGACAAAGGCT GCCCTCGACGGAGGCAATAAGCATTTCCTCAGGAATCAGCCTCTGACATTCGCTCTGCAACTGCATGACCCTAGCGGATACCTCGCCGAATGCGATGT GTGTACCGATCAGCTCTTCGGAGCCGCTAGGCCTGACGATCCCACACTGATTAGCAGAAACTCCAGGTTTAGCTCCTGGGAAGCCGCTATGCCTAGGG AAGACGCTCACTTTATCTATGGCTATCCCAAAAAGGGACACGGGACACTCCTACACAACCGCTGAGGAAGCCGCTACCGGAAAGTATGACCCTGCCGTC TCGCCAAAAAGAGAGTGCATCCCGATTACGTCACACCCCAACACTGGTTCTTTGCCTATCTGACACTGGCTAAGCATACCATTAGCTCCGACTAT GTGATTCCCATTGGCACATACGGACAGATGAAGAATGGCTCCGGCACAAACGTCCTGGAAACGCTGTGATTCTGCTCCTGGAAGCCGGAGCCCTGGT GAAAGAATTACGGACAGCTCGACATTTGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAGTGTCCCTGCAAGAGAAAAACTGTGAGCCTGTGGTC GCCTGCCTCCGACGAATGGATGAAGAGATTCAATCCCCCTGCCGATGCCTGGCCCCAAGAGCTCGCCCCTATCGGACACAATAGGATGTACAATATGG TCGCCTTTCACTCCCAGGAACTGAGAAGGACACTGAAAGAGGTCCTGACATGCTCCTGGGCTGCCTTCTCCCACCAAGGCCCTGCCTTTGTGACATGG CATAGGTATCACCTCCTGTGTCTGGAAAGGGATCTGCAAAGGCTCATCGGAAACGGAAAGGCCTATGGTCCAGAGACTGCCTCAGGATCTGGC TCAGTGTCTGGAAGTGGGACTGTTTGACACACCCCCTTTCTATAGCAATCAGGATCCCATTTTCGTCCTGCTCCACACATTCACAGACGCTGTGTTTG ACGAATGGCTCAGGAGATACAATGCCGATATCTCCACCTTTCTGGGAGCCGAAAGCGCTAACGTCTGCGGAAGCCAACAGGGAAGGGGACAGTGTACC GAAGTGAGAGCCGATACCAGACCCTGGAGCGGATACAATTGCGGAGACTGTAAGTTTGGCTGGACCGGACCCAATTGCGAAAGGAAAAAGCCTCCCGT CCTTTACCGATGCCGTCGGCCTCGTGTCCCTGCTGCAGACACAAAAGGAAACAGCTCCCCGAAGAGAAAACAGCCTCTGCTCATGGAAAAGGAAGAC TATCACTCCGGCTGTAAGATTCTGCCTGGCGCTCAGGGACAGTTTCCCAGAGTGTGTATGACAGTGGATAGCCTCGTGAATAAGGAATGCTGTCCCAG GCCCTTGCCCTAGCGGAAGCTGGAGCCAAAAGAGAGCTTTGTGTATGTGTGGGAAGACATGGGGACAGTATTGGCAAGTGCTCAACCAAGACTGGCTG TCACGAAGCCCCTGCCTTTCTGCCTTGGCATAGGCTCTTCCTCCTGAGATGGGAACAGGAAATCCAAGCCGCTATGACACCCGGAACCCAAAGCCCTT TCTTTCTGCTCCTGACAGTGCTCACCGTCGTGACAGGCTCCGGCCATGCCTCCGACAAAAGCCTCCACGTCGGCACACAGTGTGCCCTCACC AGAAGGTGTCCCCAAGAGGGGATTCGATCACAGAGACTCCAAGGTCAGCCTCAACGTCACCTCCGGCTCCGGCTCCGGCTCCGGCTCCGCCTCCACCCTCGTGCATAACGGAACCTCCGCCAGAGCCACAACCACACCCGCTCTGGAAGGCTTTGCCTCCCCCCTCACCGGAATCGCTGACGCTAGCCAAAGCTCCA TGCATAACGCTCTGCATATCTATATGAATGGCACAAGGGATACCCTCCTGGGACCCGGAAGGCCTTACAGAGCCATTGACTTTAGCCATCAGGGACCC GCTTTCGTCACCTGGCACAGATACCATGCCGCTATGCTCCTGGCTGTGCTCTACTGTCTGCTCTGGTCCTTCCAAACCTCCGCCGGACACTTTCCCAG AGCCTGTGTGTCCAGCAAAGCCTTTGAGCTCACCGTCAGCTGTCAGGGAGGCCTCCCCAAAGAGGCTTGCATGGAGATTAGCTCCCCCGGATGCCAAC $\tt CCCCTGCCCAAGTGGATGACAGAGGTCCTGGCCTAGCGTCTTCTATAACAGAACCTGTCAGTGTAGCGGAAACTTTATGGGATTCAATTGCGGAAAC$ TGTGAGTCCGCCGAAATCCTCCAGGCTGTGCCTAGCGGAGAGGGGAGACGCTTTCGAACTGACAGTGTCCTGCCAAGGCGGACTGCCTAAGGAAACCGT CTGCGATAGCCTCGACGATTACAATCACCTCGTGACACTGTGTAACGGAACCTATGAGGGACTGCTCAGGAGAAACCAAATGGGACTGCTCAGCAATG CCCCTCTGGGACCCCAATTCCCTTTCACAGGCGTCGACGATAGGGAAAGCTGGCCCTCCGTGTTTTACAATAGGACATACGAAAAGCTCAGCGCTGAG GAAACAGGATTTCTCCGTGCCTGGCATTGGCATTCTGACAGTGATTCTGGGAGTGCTCCTCCTCATCGGATGCTGGTACTGTAGGAGAAGGAATGGCT ATAGGGCTCTGATGTACTCCTACCTCCAGGATAGCGATCCCGATAGCTTTCAGGATTACATTAAGTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCC TGGCTCCAGGGACAGGATGTGACACTGGCTCCCGCTACCGAACCCGCTAGCGGAAGCGCTGCCACATGGGGACAGGATGTGACAAGCGTCCCCGTCAC CTCCTGCGGAAGCTCCCCCGTCCCCGGAACCACAGACGGACACAGACCCCACAGCCGGAAGCCCCTAACACCGCTGGCCAAGTGCCTCTGGTCCACA CCCACAACCCTCCTGGTCGTGATGGGCACACTGGTCGCCCTCGTGGGACTGTTTGTGCTCCTGGCTTTCCTCACCACAACCGAATGGGTCGAGACAAC CGCTAGGGAACTGCCTATCCCTGAGCCTGAGGGACCCGATGCCTCCAGCATTATGTCCACCGAAGGCGCTGTGACACTGACAATCCTCCTGGGAATCT TTTTCCTCTGCTGGGGCCCTTTCTTCTGCATCTGACACTGATTGTCCTCTGCCCCTCTGGGAGCCGCTATGGTCGGCGCTGTGCTCACCGCTCTGCTC GCCGGACTGGTCAGCCTCCTGTGTAGGCATAAGAGAAAGCAACTGCCTGGCGCTCTGGTCGCCAGAGCCGCTGTGCTCCAGCAACTGGATAACGTCAT CGATGTGATTACCTGTAGCTCCATGCTCAGCTCACCTGTGTATGACACCCGGAAAAGGTCCCCGTCAGCGAAAGTGATGGCCACAACCCTCGCCGGAAATGT $\tt CCACCCCTGAGGCTACCGGAATGACACCCGCTCAGACAAGCGCTGGCCATTTCCCTAGGGCTTGCGTCAGCTCCAAGAATCTGATGGAGAAGAGTGT\\$ TGCCCTCCCTGGAGCGGAGACAGAGCCCTCAGGTATCACTCCATCGTCACCCTCCCCAGAGCCCCTAGGGCTGTGGCTGCCATTTGGGTCGCCTCCGT GGTCTTCTCCACCTCTTCAGAGAGGGAACCATTAACGTCCACGATGTGGAAACCCAATTCAATCAGTATAAGACAGAGGCTGCCTCCAGGTATAACC TCACCATTAACCTCATGGAAAAGGAATGCTGTCCCCCTTGGTCCGGCGATAGGTCCCCCTGTGGCCAACTGTCCGGCAGAGGCTCCTGCCAAAACATT CTGGCTGGGGCATTGCCCTCCTGGTCCTGGTCTGGTCCTGGTCGCCCATTGTGTATCTGATTGCCCTCTTCCTCGGCGCTATCGCTGTGGAT AGGTATATCTCCATCTTTTACGCTCTGAGATACCATAGCATTGTGACACTGCCTAGGGCTCCCAGACTGATTATGCCTGGCCAAGAGGCTGGCCTCGG TTCTGCAATACAGAAGGCTCAGGAAAGGCTATACCCCTCTGATGGAGACACTGATTAGCCCTAACTCCGTGTTTAGCCAATGGAGAGTGGTCTGCGAT AGCCTCGAGGATTACGATACCCTCGGCACACTGTGTAACTCCCTGAATAGCACACCCACAGCCATTCCCCAACTGGGACTGGCTACCCAATCAGACAGG CGCTAGGTGTCTGGAAGTGTCCATCTCCGACGGACACAGACCCCTCCAGGAAGTGTATCCCGAAGCCAATGCCCCTATCGGACACAATAGGGAAAGCT

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ATATGGTCCCTTTATCCTCTGTATGAGCCTAGCGGAACCACAAGCGTCCAGGTCCCACAACCGAAGTGATTAGCACAGCCCTGTGCAAATGCCT
ACCGCTGAGTCCACCGGAAAGAAAAGGGTCCACCCTGACTAGTGATTACCACACAGCATTGGCTCGGCCTCCTGGGACCCAATGGCACACAGCCTCA
GTTTGCCAATCTGCATCAGATTCTGAAAGGCGGAACCGGAACCTATTGCCTCAACGTCAGCCTCGCCGATACCAATAGCCTCGCCGTCGTGTCCACCC
AACCCGAAGCCCGAAGGCCTTAGCTCCATCATGAGGCACAGAGTCCATCACAGGCTCCTTGGGACCCCTCCTGGATGGCACAGCCACAGCATT
ACCGGAAGCCTCGGCCCTCTGCTCGACGGAACCGCTACCCTCCAGGCTCGTGAAAAGGCAAGTGCCTCTGGATTGCCTCTGTATGACTGTTGGAGAGG
CGGACAGGTCAGCCTCAAGGTCAGCAATGACGGACCCACACTGATTGGCGCTTAACGCTTAGCATTTGCCCTC

```
Melanoma cancer Specific Savine Scramble process
Scramble - Output File
Scramble version: 0.1 beta, 08/02/1999
Num. genes : 10
Num. segments : 121
Segment length : 30
Segment overlap : 15
Segments in original order:
        : BAGE
Segment# : 1
Offset
       : 1
1st Codon : 1
 A A M A A R A V F L A L S A Q L L Q A R L M K E E S P V V S
: BAGE
Segment# : 2
Offset
       : 16
1st Codon : 1
 LLQARLMKEESPVVSWRLEPBDGTALCFIF
CTGCTCCAGGCTAGGCTCATGAAAGAGGAAAGCCCTGTGGTCAGCTGGAGGCTCGAGCCTGAGGATGGCACAGCCCTCTGCTTTATCTTT
        : BAGE
Gene
Segment# : 3
Offset
       : 31
1st Codon : 1
 WRLEPEDGTALCFIFAA
TGGAGACTGGAACCCGAAGACGGAACCGCTCTGTGTTTCATTTTCGCTGCC
Gene-
       : GAGE-1
Segment# : 1
Offset : 1
1st Codon : 1
A A M S W R G R S T Y R P R P R R Y V E P P E M I G P M R P
GCCGCTATGTCCTGGAGAGGCCAGAAGCACATACAGACCCAGAACCCAGAAGGTATGTGGAACCCCTGAGATGATCGGACCCATGAGGCCT
Segment# : 2
Offset
       : 16
1st Codon : 1
RRYVEPPBMIGPMRPEQFSDEVEPATPEEG
AGGAGATACGTCGAGCCTCCCGAAATGATTGGCCCTATGAGACCCGAACAGTTTAGCGATGAGGTCGAGCCTGCCACACCCGAAGAGGGA
Gene
       : GAGE-1
Segment# : 3
       : 31
Offset
1st Codon : 1
EQFSDEVEPATPEEGEPATQRQDPAAAQEG
GAGCAATTCTCCGACGAAGTGGAACCCGCTACCCCTGAGGAAGGCGAACCCGCTACCCAAAGGCAAGACCCTGCCGCTGCCCAAGAGGGA
Gene
       : GAGE-1
Segment# : 4
Offset
       : 46
1st Codon : 1
EPATQRQDPAAAQEGEDEGASAGQGPKPBA
GAGCCTGCCACACAGAGACAGGATCCCGCTGCCGCTCAGGAAGGCGAAGACGAAGGCGCTAGCGCTAGGCCAAGGCCCTAAGCCTGAGGCT
       : GAGE-1
Segment# : 5
Offset : 61
1st Codon : 1
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```
E D E G A S A G Q G P K P E A D S Q E Q G H P Q T G C E C E
 GAGGATGAGGGAGCCTCCGCCGGACAGGGACCCAAACCCGAAGCCGATGCCGAAGCCAAGGCCATCCCCAAACCGGATGCGAATGCGAA
         : GAGE-1
 Gene
 Segment# : 6
         : 76
 Offset
 1st Codon : 1
  D S Q E Q G H P Q T G C E C E D G P D G Q E M D P P N P E E
 GACTCCCAGGAACAGGGACACCCTCAGACAGGCTGTGAGTGTGAGGATGGCCCTGACGGACAGGAAATGGATCCCCCTAACCCTGAGGAA
 Gene
         : GAGE-1
 Segment# : 7
 Offset
         : 91
 1st Codon : 1
 D G P D G Q B M D P P N P B B V K T P B B B M R S H Y V A Q
 GACGGACCCGATGGCCAAGAGATGGACCCTCCCAATCCCGAAGAGGGTCAAGACACCCCGAAGAGGGAAATGAGAAGCCATTACGTCGCCCAA
 Gene
         : GAGE-1
 Segment# : 8
 Offset
        : 106
 1st Codon : 1
 V K T P E E B M R S H Y V A Q T G I L W L L M N N C F L N L
 GTGAAAACCCCTGAGGAGGAGGAGGTCCCACTATGTGGCTCAGACAGGCATTCTGTGGCTGCTCATGAATAACTGTTTCCTCAACCTC
         : GAGE-1
 Gene
 Segment# : 9
 Offset
 1st Codon : 1
 T G I L W L L M N N C P L N L S P R K P A A
ACCGGAATCCTCTGGCTCCTGATGAACAATTGCTTTCTGAATCTGTCCCCCAGAAAGCCTGCCGCT
Gene
         : gp100In4
Segment# : 1
Offset
        : 1
1st Codon : 1
 A A S W S Q K R S F V Y V W K T W G B G L P S Q P I I H T C
GCCGCTAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGGAAGACATGGGGAGAGGGACTGCCTAGCCAACCCATTATCCATACCTGT
Gene
        : qp100In4
Segment# : 2
Offset
        : 16
1st Codon : 1
 T W G E G L P S Q P I I H T C V Y F F L P D H L S F G R P F
ACCTGGGGCGAAGGCCTCCCCAGCCTATCATTCACACATGCGTCTACTTTTTCCTCCCCGATCACCTCAGCTTTGGCAGACCCTTT
Gene
        : gpl00In4
Segment# : 3
Offset
        : 31
1st Codon : 1
 V Y F F L P D H L S F G R P F H L N F C D F L A A
GTGTATTTCTTCTGCCTGACCATCTGTCCTTCGGAAGGCCTTTCCATCTGAATTTCTGTGACTTTCTGGCTGCC
        : MAGE-1
Gene
Segment# : 1
Offset
1st Codon : 1
A A M S L E Q R S L H C K P E E A L B A Q Q E A L G L V C V
GCCGCTATGTCCCTGGAACAGAGAAGCCTCCACTGTAAGCCTGAGGAAGCCCTCGAGGCTCAGCAAGAGGCTCTGGGACTGGTCTGCGTC
Gene
        : MAGE-1
Segment# : 2
Offset
1st Codon : 1
B A L B A Q Q B A L G L V C V Q A A T S S S P L V L G T L
Gene
        : MAGE-1
Segment# : 3
Offset
       : 31
1st Codon : 1
Q A A T S S S P L V L G T L B B V P T A G S T D P P Q S P
CAGGCTGCCACAAGCTCCAGGTCCCCCTCGTGCTCGGCACACTGGAAGAGGTCCCCACAGCCGGAAGCACAGACCCTCCCCAAAGCCCT
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: MAGE-1 Segment# : 4 Offset : 46 1st Codon : 1 B B V P T A G S T D P P Q S P Q G A S A F P T T I N F T R Q : MAGE-1 Segment# : 5 Offset : 61 1st Codon : 1 Q G A S A F P T T I N F T R Q R Q P S B G S S S R B B B G P CAGGGAGCCTCCGCCTTTCCCACAACCATTAACTTTACCAGACAGGACAGCCTAGCGAAGGCTCCAGCTCCAGGGAAGAGGACGCCCT : MAGE-1 Gene Segment# : 6 Offset : 76 1st Codon : 1 RQPSEGSSSREBEGPSTSCILBSLFRAVIT : MAGE-1 Gene Segment# : 7 Offset : 91 1st Codon : 1 STSCILESLFRAVITKKVADLVGFLLLKYR' AGCACAAGCTGTATCCTCGAGTCCCTGTTTAGGGCTGTGATTACCAAAAAGGTCGCCGATCTGGTCGGCTTTCTGCTCCTGAAATACAGA : MAGE-1 Segment# : 8 Offset 1st Codon : 1 K K V A D L V G F L L K Y R A R B P V T K A B M L B S V I AAGAAAGTGGCTGACCTCGTGGGATTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGAGTCCGTGATT Gene : MAGE-1 Segment# : 9 Offset AREPVTKAEMLESVIKNYKHCFPEIFGKAS GCCAGAGAGCCTGTGACAAAGGCTGAGATGCTGGAAAGCGTCATCAAAAACTATAAGCATTGCTTTCCCGAAATCTTTGGCAAAGCCTCC : MAGE-1 Gene Segment# : 10 : 136 Offset 1st Codon : 1 K N Y K H C F P E I F G K A S E S L Q L V F G I D V K E A D AAGAATTACAAACACTGTTTCCCTGAGATTTTCGGAAAGGCTAGCGAAAGCCTCCAGCTCGTGTTTGGCATTGACGTCAAGGAAGCCGAT : MAGE-1 Gene Segment# : 11 Offset : 151 ESLQLVFGIDVKEADPTGHSYVLVTCLGLS GAGTCCCTGCAACTGGTCTTCGGAATCGATGTGAAAGAGGCTGACCCTACCGGACACTCCTACGTCCTGGTCACCTGTCTGGGACTGTCC Gene : MAGE-1 Segment# : 12 Offset : 166 1st Codon : 1 PTGHSYVLVTCLGLSYDGLLGDNQIMPKTG CCCACAGGCCATAGCTATGTGCTCGTGACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAACCAAATCATGCCCAAAACCGGA Gene : MAGE-1 Segment# : 13 Offset : 181 1st Codon : 1 Y D G L L G D N Q I M P K T G P L I I V L V M I A M E G G H Gene : MAGE-1

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Segment# : 14 Offset : 196 1st Codon : 1 PLIIV L V M I A M E G G H A P E E E I W E E L S V M E V TTCCTCATCATCGTGGTGGTGATGGTCGCTATGGAAGGCGGACACGCTCCCGAAGAGGGAAATCTGGGAGGAACTGTCCGTGATGGAGGTC : MAGE-1 Segment# : 15 Offset : 211 1st Codon : 1 APEEELS V M E V Y D G R E H S A Y G E P R K L GCCCCTGAGGAAGAGATTTGGGAAGAGCTCAGGGTCATGGAAGTGTATGACGGAAGGGAACACTCCGCCTATGGCGAACCCAGAAAGCTC : MAGE-1 Gene Segment# : 16 Offset : 226 1st Codon : 1 Y D G R E H S A Y G E P R K L L T Q D L V Q E K Y L E Y R Q TACGATGCCAGAGAGCATAGCGCTTACGGAGAGCCTAGGAAACTGCTCACCCAAGACCTCGTGCAAGAGAAATACCTCGAGTATAGGCAA : MAGE-1 Gene Segment# : 17 Offset : 241 1st Codon : 1 LTQDLVQEKYLBYRQVPDSDPARYBFLWGP : MAGE-1 Segment# : 18 : 256 Offset 1st Codon : 1 V P D S D P A R Y E F L W G P R A L A B T S Y V K V L B Y V GTGCCTGACTCCGACCCTGCCAGATACGAATTCCTCTGGGGACCCAGAGCCCTCGCCGAAACCTCCTACGTCAAGGTCCTGGAATACGTC Gene : MAGE-1 Segment# : 19 : 271 1st Codon : 1 RALAETSYVKVLKYVIKVSARVRFFFPSLR : MAGE-1 Gene Segment# : 20 Offset : 286 1st Codon : 1 I K V S A R V R F F F P S L R E A A L R E E E G V A A ATCAAAGTGTCCGCCAGAGTGAGATTCTTTTTCCCTAGCCTCAGGGAAGCCGCTCTGAGAGAGGAAGAGGAAGGCGTCGCCGCT Gene ' : MAGE-3 Segment# : 1 Offset : 1 1st Codon: 1 A A M P L B Q R S Q H C K P B B G L B A R G B A L G L·V G A GCCGCTATGCCTCTGGAACAGAGAGACACACTGTAAGCCTGAGGAAGGCCTCGAGGCTAGGGGGAGAGGCTCTGGGACTGGTCGGCGCT Segment# : 2 Offset : 16 1st Codon: 1 B G L B A R G B A L G L V G A Q A P A T B B Q B A A S S S GAGGGACTGGAAGCCAGAGGCGAAGCCCTCGGCCTCGTGGGAGCCCAAGCCCCTGCCACAGAGGAACAGGAAGCCGCTAGCTCCAGCTCC : MAGE-3 Gene Segment# : 3 Offset : 31 1st Codon : 1 Q A P A T B E Q B A A S S S S T L V B V T L G B V P A A B S Gene : MAGE-3 Segment# : 4

Figure 27 (Cont)

Offset

187/216

1st Codon : 1 TLVRVTLGEVPAABSPDPPQSPQGASSLPT ACCUTEGTGGAAGTGACACTGGGAGAGGTCCCCGCTGCCGAAAGCCCTGACCCTCCCCAAAGCCCTCAGGGAGCCTCCAGCCTCCCACA : MAGE-3 Gene Segment# : 5 Offset 1st Codon : 1 P D P P Q S P Q G A S S L P T T M N Y P L W S Q S Y E D S S CCCGATCCCCTCAGTCCCCCAAGGCGCTAGCTCCCTGCCTACCACAATGAATTACCCTCTGTGGAGCCAAAGCTATGAGGATAGCTCC Gene : MAGE-3 Segment# : 6 1st Codon : 1 T M N Y P L N S Q S Y E D S S N Q E E E G P S T P P D L E S ACCATGAACTATCCCCTCTGGTCCCAGTCCTACGAAGACTCCAGCAATCAGGAAGAGGAAGGGCCCTAGCACATTCCCTGACCTCGAGTCC : MAGE-3 Gene Segment# : 7 Offset : 91 1st Codon : 1 NQBEEGPSTPPDLESEPQAALSRKVABLVH AACCAAGAGGAAGAGGGACCCTCCACCTTTCCCGATCTGGAAAGCGAATTCCAAGCCGCTCTGTCCAGGAAAGTGGCTGAGCTCGTGCAT : MAGE-3 Gene Segment# : 8 Offset : 106 1st Codon : 1 E F Q A A L S R K V A E L V H F L L K Y R A R E P V T K A GAGTTTCAGGCTGCCCTCAGCAGAAAGGTCGCCGAACTGGTCCACTTTCTGCTCCTGAAATACAGAGCCAGAGAGCCTGTGACAAAGGCT Gene : MAGE-3 Segment# : 9 Offset : 121 1st Codon : 1 P L L K Y R A R E P V T K A E M L G S V V G N N Q Y F P P TTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGGCTCCGTCGGCAATTGGCAATTACTTTTCCCT Segment# : 10 Offset : 136 1st Codon : 1 B M L G S V V G N W Q Y F F P V I F S K A S S S L Q L V F G Gene : MAGE-3 Segment# : 11 Offset : 151 1st Codon : 1 V I F S K A S S S L Q L V F G I E L M E V D P I G H L Y I F GTGATTTTCTCCAAGGCTAGCTCCAGCCTCCAGCTCGTGTTTGGCATTGAGCTCATGGAAGTGGATCCCATTGGCCATCTGTATATCTTT Gene : MAGE-3 Segment# : 12 Offset : 166 1st Codon : 1 I E L M E V D P I G H L Y I P A T C L G L S Y D G L L G D N ATCGAACTGATGGAGGTCGACCCTATCGGACACCTCTACATTTTCGCTACCTGTCTGGGACTGTCCTACGATGGCCTCCTGGGAGACAAT Gene : MAGE-3 Segment# : 13 Offset 1st Codon : 1 A T C L G L S Y D G L L G D N Q I M P K A G L L I I V L A I GCCACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAACCAAATCATGCCCAAAGCCGGACTGCTCATCATTGTGCTCGCCATT : MAGE-3 Gene Segment# : 14 Offset : 196 1st Codon : 1 Q I M P K A G L L I I V L A I I A R E G D C A P E B K I W B

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```
Gene
        : MAGE-3
 Segment# : 15
 Offset
       : 211
 1st Codon : 1
 I A R B G D C A P B B K I W B B L S V L E V F E G R E D S I
 ATCGCTAGGGAAGGCGATTGCGCTCCCGAAGAGAAAATCTGGGAGGAACTGTCCGTGCTCGAGGTCTTCGAAGGCAGAGAGGATAGCATT
Gene
        : MAGE-3
Segment# : 16
Offset
       : 226
1st Codon : 1
 ELSVLEVFEGREDSILGOPKKLLTOHFVOE
GAGCTCAGCGTCCTGGAAGTGTTTGAGGGAAGGGAAGACTCCATCCTCGGCGATCCCAAAAAGCTCCTGACACAGCATTTCGTCCAGGAA
Gene
       : MAGE-3
Segment# : 17
Offset
       : 241
1st Codon : 1
 LGDPKKLLTQHPVQENYLEYRQVPGSDPAC
: MAGE-3
Gene
Segment# : 18
Offset
       : 256
1st Codon : 1
 N Y L E Y R Q V P G S D P A C Y E F L W G P R A L V E T S Y
AACTATCTGGAATACAGACAGGTCCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCTAGGGCTCTGGTCGAGACAAGCTAT
       : MAGE-3
Gene
Segment# : 19
Offset
       : 271
1st Codon : 1
 Y R F L W G P R A L V E T S Y V K V L H H M V K I S G G P H
TACGAATTCCTCTGGGGACCCAGAGCCCTCGTGGAAACCTCCTACGTCAAGGTCCTGCATCACATGGTGAAAATCTCCGGCGGACCCCAT
Gene
       : MAGE-3
Segment# : 20
Offset
1st Codon : 1
V K V L H H M V K I S G G P H I S Y P P L H E W V L R E G E
GTGAAAGTGCTCCACCATATGGTCAAGATTAGCGGAGGCCCTCACATTAGCTATCCCCCTCTGCATGAGTGGGTGCTCAGGGAAGGCGAA
       : MAGE-3
Gene
Segment# : 21
Offset
      : 301
1st Codon : 1
ISYPPLHEWVLREGERAA
Gene
       : PRAME
Segment# : 1
Offset
       : 1
1st Codon : 1
AAMERRRLWGSIQSRYISMSVWTSPRRLVR
GCCGCTATGGAAAGGAGAAGGCTCTGGGGAAGCATTCAGTCCAGGTATATCTCCATGTCCGTGTGGACCTCCCCCAGAAGGCTCGTGGAA
Gene
      : PRAME
Segment# : 2
Offset
      : 16
1st Codon : 1
Y I S M S V W T S P R R L V E L A G Q S L L K D E A L A I A
TACATTAGCATGAGGGTCTGGACAAGCCCTAGGAGACTGGTCGAGCTCGCCGGACAGTCCCTGCTCAAGGATGAGGCTCTGGCTATCGCT
Gene
       : PRAME
Segment# : 3
Offset
      : 31
1st Codon : 1
LAGQSLLKDBALAIAALELLPRELFPLFM
CTGGCTGGCCAAAGCCTCCTGAAAGACGAAGCCCTCGCCATTGCCGCTCTTGGAACTGCTCCCCAGAGAGGCTCTTCCCCCCCTCTTCATG
```

PCT/AU01/00622 WO 01/090197

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Gene : PRAME Segment# : 4 Offset : 46 1st Codon : 1 A L B L L P R B L F P P L F M A A F D G R H S Q T L K A M V GCCCTCGAGCTCCTGCCTAGGGAACTGTTTCCCCCTCTGTTTATGGCTGCCTTTGACGGAAGGCATAGCCAAACCCTCAAGGCTATGGTC : PRAMB Gene Segment# : 5 Offset : 61 1st Codon : 1 A A F D G R H S Q T L K A M V Q A W P F T C L P L G V L M K GCCGCTTTCGATGGCAGACACTCCCAGACACTGAAAGCCATGGTGCAAGCCTTGCCCTTTACCTGTCTGCCTCTGGGAGTGCTCATGAAA : PRAME Segment# : 6 Offset 1st Codon : 1 Q A W P F T C L P L G V L M K G Q H L H L E T F K A V L D G CAGGCTTGCCCTTTCACATGCCTCCCCCTCGGCGTCCTGATGAAGGGACAGCATCTGCATCTGGAAACCTTTAAGGCTGTGCTCGACGGA : PRAME Segment# : 7 Offset : 91 1st Codon : 1 G Q H L H L E T F K A V L D G L D V L L A Q E V R P R R W K GGCCAACACCTCCACCTCGAGACATTCAAAGCCGTCCTGGATGGCCTCGACGTCCTGCTCGCCCAAGAGGTCAGGCCTAGGAGATGGAAA : PRAME Segment# : 8 Offset : 106 1st Codon : 1 LDVLLAQBVRPRRWKLQVLDLRKNSHQDFW CTGGATGTGCTCCTGGCTCAGGAAGTGAGACCCAGAAGGTGGAAGCTCCAGGTCCTGGATCTGGAAAGAATAGCCATCAGGATTTCTGG : PRAME Gene Segment# : 9 Offset 1st Codon : 1 LQVLDLRKNSHQDFWTVWSGNRASLYSFPE CTGCAAGTGCTCGACCTCAGGAAAAACTCCCACCAAGACTTTTGGACAGTGTGGAGCGGAAACAGAGCCTCCCTGTATAGCTTTCCCGAA : PRAME Gene Segment# : 10 : 136 Offset 1st Codon : 1 T V W S G N R A S L Y S P P B P E A A Q P M T K K R K V D G ACCGTCTGGTCCGGCAATAGGGCTAGCCTCTACTCCTTCCCTGAGCCTGAGGCTGCCCAACCCATGACCAAAAAGAGAAAGGTCGACGGA Gene : PRAME Segment# : 11 Offset : 151 1st Codon : 1 P B A A Q P M T K K R K V D G L S T B A B Q P F I P V B V L CCCGAAGCCGCTCAGCCTATGACAAAGAAAAGGAAAGTGGATGGCCTCAGCACAGAGGCTGAGCAACCCTTTATCCCTGTGGAAGTGCTC Gene ' : PRAME Segment# : 12 Offset : 166 1st Codon : 1 LSTEAEQPFIPVEVLVDLFLKEGACDELFS : PRAME Segment# : 13 Offset : 181 1st Codon : 1 V D L F L K B G A C D B L F S Y L I B K V K R K K N V L R L GTGGATCTGTTTCTGAAAGAGGGGAGCCTGTGACGAACTGTTTAGCTATCTGATTGAGAAAAGGAAAAAGGAAAAAGAATGTGCTCAGGCTC

: PRAME Gene Segment# : 14

190/216

Offset : 196 1st Codon : 1 Y L I B K V K R K K N V L R L C C K K L K I P A M P M Q D I TACCTCATCGAAAAGGTCAAGAAAAAACGTCCTGAGACTGTCTTGCAAAAAGCTCAAGATTTTCGCTATGCCTATGCAAGACATT : PRAME Gene Segment# : 15 Offset : 211 1st Codon : 1 C C K K L K I F A M P M Q D I K M I L K M V Q L D S I K D L TGCTGTAAGAAACTGAAAATCTTTGCCATGCCCATGCAGGATATCAAAATGATTCTGAAAATGGTCCAGCTCGACTCCATCGAAGACCTC Gene : PRAME Segment# : 16 Offset : 226 1st Codon : 1 K M I L K M V Q L D S I E D L E V T C T W K L P T L A K P S AAGATGATCCTCAAGATGGTGCAACTGGATAGCATTGAGGATCTGGAAGTGACATGCACATGGAAACTGCCTACCCTCGCCAAATTCTCC Gene : PRAME Segment# : 17 Offset : 241 E V T C T W K L P T L A K P S P Y L G Q M I N L R R L L L S GAGGTCACCTGTACCTGGAAGCTCCCCACACTGGCTAAGTTTAGCCCTTACCTCGGCCAAATGATTAACCTCAGGAGACTGCTCCTGTCC Gene : PRAME Segment# : 18 Offset : 256 1st Codon : 1 PYLGQMINLRRLLLSHIHASSYISPEKEEO CCCTATCTGGGACAGATGATCAGTCAGACAGGCTCCTGCTCAGCCATATCCATGCCTCCAGCTATATCTCCCCCGAAAAGGAAGAGCAA Gene : PRAME Segment# ;: 19 Offset : 271 1st Codon : 1 HIHASSYISPEKEEQYIAQFTSQFLSLQCL CACATTCACGCTAGCTCCTACATTAGCCCTGAGAAAGAGGGAACAGTATATCGCTCAGTTTACCTCCCAGTTTCTGTCCCTGCAATGCCTC : PRAME Gene Segment# : 20 Offset Y I A Q F T S Q F L S L Q C L Q A L Y V D S L F F L R G R L TACATTGCCCAATTCACAAGCCAATTCCTCAGCCTCCAGTGTCTGCAAGCCCTCTACGTCGACTCCCTGTTTTTCCTCAGGGGAAGGCTC Gene : PRAME Segment# : 21 : 301 Offset 1st Codon : 1 Q A L Y V D S L F F L R G R L D Q L L R H V M N P L B T L S CAGGCTCTGTATGTGGATAGCCTCTTTCTTGAGAGGCAGACTGGATCAGCTCCTGAGACACGTCATGAATCCCCTCGAGACACTGTCC : PRAME Gene Segment# : 22 Offset : 316 1st Codon : 1 D Q L L R H V M N P L B T L S I T N C R L S E G D V M H L S GACCAACTGCTCAGGCATGTGATGAACCCTCTGGAAACCCTCAGCATTACCAATTGCAGACTGTCCGAGGGAGACGTCATGCATCTGTCC : PRAME Gene Segment# : 23 Offset : 331 1st Codon : 1 I T N C R L S E G D V M H L S Q S P S V S Q L S V L S L S G ATCACAAACTGTAGGCTCAGCGAAGGCGATGTGATGCACCTCAGCCAAAGCCCTTAGCGTCAGCCAACTGTCCGTGCTCAGCCTCAGCCGGA : PRAME Gene Segment# : 24 : 346 Offset 1st Codon : 1

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```
Q S P S V S Q L S V L S L S G V M L T D V S P E P L Q A L L
 : PRAME
 Gene
 Segment# : 25
 Offset
        : 361
 1st Codon : 1
  V M L T D V S P B P L Q A L L B R A S A T L Q D L V P D B C
 GTGATGCTGACAGACGTCAGCCCTGAGCCCTCTGCAAGCCCTCCTGGAAAGGGCTAGCGCTACCCTCCAGGATCTGGTCTTCGATGAGTGT
        : PRAME
 Gene
 Segment# : 26
 Offset
        : 376
 1st Codon : 1
 ERASATLQ DLV PDECGITDDQ LLALL PS LS
 GAGAGAGCCTCCGCCACACTGCAAGACCTCGTGTTTGACGAATGCGGAATCACAGACGATCAGCTCCTGGCTCTCCCTGTCC
 Gene
        : PRAME
 Segment# : 27
 1st Codon : 1
 G I T D D Q L L A L L P S L S H C S Q L T T L S F Y G N S I
 GGCATTACCGATGACCAACTGCTCGCCCTCCTGCCTAGCCTCAGCCATTGCTCCCAGCTCACCACACTGTCCTTCTATGGCAATAGCATT
        : PRAME
 Gene
 Segment# : 28
 Offset
1st Codon : 1
 H C S Q L T T L S F Y G N S I S I S A L Q S L L Q H L I G L
CACTGTAGCCAACTGACAACCCTCAGCTTTTACGGAAACTCCATCTCCATCTCCGCCCTCCAGTCCCTGCTCCAGCATCTGATTGGCCTC
        : PRAME
Gene
Segment# : 29
Offset
        : 421
1st Codon : 1
 S I S A L Q S L L Q H L I G L S N L T H V L Y P V P L E S Y
AGCATTAGCGCTCTGCAAAGCCTCCTGCAACACCTCATCGGACTGTCCAACCTCACCCATGTGCTCTACCCTGTGCCTCTGGAAAGCTAT
Gene
        : PRAME
Segment# : 30
Offset
       : 436
1st Codon : 1
 S N L T H V L Y P V P L E S Y E D I H G T L H L E R L A Y L
AGCAATCTGACACACGTCCTGTATCCCGTCCCCCTCGAGTCCTACGAAGACATTCACGGAACCCTCCACCTCGAGAGACTGGCTTACCTC
Gene
        : PRAME
Segment# : 31
       : 451
1st Codon : 1
 B D I H G T L H L E R L A Y L H A R L R E L L C E L G R P S
GAGGATATCCATGCCACCTGCATCTGGAAAGGCTCGCCTATCTGCATGCCAGACTGAGAGAGCTCCTGTGTGAGCTCGGCAGACCCTCC
        : PRAME
Gene
Segment# : 32
Offset
       : 466
1st Codon : 1
 HARLRBLLCELGRPSMVWLSANPCPHCGDR
CACGCTAGGCTCAGGGAACTGCTCTGCGAACTGGGAAGGCCTAGCATGGTGTGGCTGTCCGCCAATCCCTGTCCCCCATTGCGGAGACAGA
        : PRAME
Gene
Segment# : 33
Offset
       : 481
1st Codon : 1
MVWLSANPCPHCGDRTFYDPEPILCPCFMP
ATGGTCTGGCTCAGCGCTAACCCTTGCCCTCACTGTGGCGATAGGACATTCTATGACCCTGAGCCTATCCTCTGCCCTTGCTTTATGCCT
       : PRAME
Gene
Segment# : 34
Offset
       : 496
1st Codon : 1
T F Y D P B P I L C P C F M P N A A
ACCTTTTACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCCAATGCCGCT
```

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: TRP2IN2 Gene Segment# : 1 1st Codon : 1 A A L M E T H L S S K R Y T E E A G G F F P W L K V Y Y Y R GCCGCTCTGATGGAGACACACCTCAGCTCCAAGAGATACACAGAGGGAAGCCGGAGGCTTTTTCCCTTGGCTCAAGGTCTACTATTACAGA : TRP2IN2 Gene Segment# : 2 Offset : 16 1st Codon : 1 BAGGFFPWLKVYYYRPVIGLRVWQWEVISC GAGGCTGGCGGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTTGTGATTGGCCTCAGGGTCTGGCAATGGGAAGTGATTAGCTGT : TRP2IN2 Segment# : 3 Offset : 31 1st Codon : 1 PVIGLRV W Q W B V I S C K L I K R A T T R Q P A A TTCGTCATCGGACTGAGÀGTGTGGCAGTGGGAGGTCATCTCCTGCAAACTGATTAAGAGAGCCACAACCAGACAGCCTGCCGCT : NYNSOla Gene Segment# : 1 1st Codon : 1 A A M Q A B G R G T G G S T G D A D G P G G P G I P D G P G GCCGCTATGCAAGCCGAAGGCAGAGGCACAGGCGGAAGCACGGCGGATGCCGATGCCCTGGCGGACCCGGAATCCCTGACGGACCCGGA : NYNSO1a Gene Segment# : 2 Offset : 16 D A D G P G G P G I P D G P G G N A G G P G E A G A T G G R GACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGCCCTGGCGGAAACGCTGGCGGACAGGCTGGCGTTACCGGAGGCAGA : NYNSOla Gene Segment# : 3 Offset : 31 1st Codon : 1 G N A G G P G E A G A T G G R G P R G A G A A R A S G P G G GGCAATGCCGGAGGCCCTGGCGAAGCCGGAGCCACAGGCGGAAGGGGACCCAGAGGCGCTGGCGAGAGCCTCCGGCCCTGGCGGA Gene : NYNSO1a Segment# : 4 Offset : 46 1st Codon : 1 G P R G A G A A R A S G P G G G A P R G P H G G A A S G L N GGCCCTAGGGGAGCCGGAGCCGCTAGGGGACCCGGAGCCGGAGCCCCTAGGGGACCCCCATGGCGGAGCCGCTAGCGGACTGAAT Gene : NYNSOla Segment# : 5 : 61 1st Codon : 1 G A P R G P H G G A A S G L N G C C R C G A R G P E S R L L GGGGCTCCCAGAGGCCCTCAGGGAGGCGCTCCCCCCGGCCTCAACGGATGCTGTAGGTGTGGCGCTAGGGGACCCGAAAGCAGACTGCTC Gene : NYNSOla Segment# : 6 Offset : 76 1st Codon : 1 G C C R C G A R G P E S R L L E F Y L A M P F A T P M E A E GGCTGTTGCAGATGCGGAGCCAGAGGCCCTGAGTCCAGGCTCCTGGAATTCTATCTGGCTATGCCTTTCGCTACCCCTATGGAAGCCGAA : NYNSOla Gene Segment# : 7 : 91 Offset 1st Codon : 1 E F Y L A M P F A T P M E A E L A R R S L A Q D A P P L P V GAGTTTTACCTCGCCATGCCCTTTGCCACACCCATGGAGGCTGAGCTCGCCAGAAGGTCCCTGGCTCAGGATGCCCCTCCCCCTCCCCGTC Gene : NYNSOla

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```
Segment# : 8
 Offset
        : 106
 1st Codon : 1
 LARRSLAQDAPPLPVPGVLLKEFTVSGNIL
 CTGGCTAGGAGAAGCCTCGCCCAAGACGCTCCCCCTCTGCCTGTGCCTGGCGTCCTGCTCAAGGAATTCACAGTGTCCGGCAATATCCTC
        : NYNSO1a
 Gene
 Segment# : 9
 Offset
 1st Codon : 1
 PGVLLKEFTVSGNILTIRLTAADHRQLQLS
 {\tt CCCGGAGTGCTCCTGAAAGAGTTTACCGTCAGCGGAAACATTCTGACAATCAGACTGACAGCCGCTGACCATAGGCAACTGTCC}
 Gene
        : NYNSOla
 Segment# : 10
 Offset
        : 136
 1st Codon : 1
 TIRLTAADHRQLQLSISSCLQQLSLLMWIT
ACCATTAGGCTCACCGCTGCCGATCACAGACAGCTCCAGCTCAGCCATTAGCTCCTGCCTCCAGCAACTGTCCCTGCTCATGTGGATCACA
Gene : NYNSOla
Segment# : 11
Offset
        : 151
1st Codon : 1
 I S S C L Q Q L S L L M W I T Q C F L P V F L A Q P P S G Q
: NYNSO1a
Gene
Segment# : 12
Offset
       : 166
1st Codon : 1
 QCFLPVFLAQPPSGQRRAA
CAGTGTTTCCTCCCCGTCTTCCTCGCCCAACCCCCTAGCGGACAGAGAGGGCTGCC
       : NYNSO1b
Segment# : 1
Offset
       : 1
1st Codon : 1
 A A M L M A Q E A L A F L M A Q G A M L A A Q E R R V P R A
GCCGCTATGCTCATGGCTCAGGAAGCCCTCGCCTTTCTGATGGCCCAAGGCGCTATGCTCGCCGCTCAGGAAAGGAGAGTGCCTAGGGCT
Gene
        : NYNSO1b
Segment# : 2
Offset
       : 16
Q G A M L A A Q B R R V P R A A B V P G A Q G Q Q G P R G R
CAGGGAGCCATGCTGGCTGCCCAAGAGAGAGGGTCCCCAGAGCCGCTGAGGTCCCCGGAGCCCAAGGGCCAACAGGGACCCAGAGGCAGA
Gene
       : NYNSO1b
Segment# : 3
Offset
       : 31
1st Codon : 1
A B V P G A Q G Q Q G P R G R B B A P R G V R M A A R L Q G
GCCGAAGTGCCTGGCGCTCAGGGACAGCAAGGCCCTAGGGGAAGGGGAAGAGGCTCCCAGAGGCGTCAGGATGGCCGCTAGGCTCCAGGGA
       : NYNSO1b
Gene
Segment# : 4
Offset
       : 46
1st Codon : 1
BBAPRGVRMAARLQGAA
GAGGAAGCCCCTAGGGGAGTGAGAATGGCTGCCAGACTGCAAGGCGCTGCC
Gene
       : LAGE1
Segment# : 1
Offset
A A M Q A B G Q G T G G S T G D A D G P G G P G I P D G P G
GCCGCTATGCAAGCCGAAGGCCAAGGCACAGGCGGAAGCACAGGCGGATGCCGGATGCCCTGGCGGACCCGGAATCCCTGACGGACCCGGA
Gene
       : LAGE1
Segment# : 2
Offset
```

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```
1st Codon : 1
  D A D G P G G P G I P D G P G G N A G G P G B A G A T G G R
 GACGCTGACCGGACCCCTGGCATTCCCGATGCCCTGGCGGAAACGCTGGCGGACACGCGAGAGGCTGGCCTACCGGAGGCAGA
 Gene
         : LAGE1
 Segment# : 3
 Offset
        : 31
 1st Codon : 1
  G N A G G P G B A G A T G G R G P R G A G A R A S G P R G
 GGCAATGCCGGAGGCCCTGGCGAAGCCGGAGCCACAGGCGGAAGGGGGACCCAGAGGCGCTGGCGCTGCCAGAGCCTCCGGCCCTAGGGGA
 Gene
        : LAGE1
 Segment# : 4
        : 46
 Offset
 1st Codon : 1
 G P R G A G A A R A S G P R G G A P R G P H G G A A S A Q D
 GGCCCTAGGGGAGCCGGAGCCGCTAGGGCTAGCGGACCCAGAGGCGGAGCCCCTAGGGGAGCCCCATGGCGGAGCCGCTAGCGCTCAGGAT
 Gene
        : LAGE1
 Segment# : 5
 Offset
        : 61
 1st Codon : 1
 G A P R G P H G G A A S A Q D G R C P C G A R P D S R L L
 GGCGCTCCCAGAGGCCCTCACGGAGGCGCTGCCTCCGCCCAAGACGGAAGGTGTCCCTGTGGCGCTAGGAGACCCGATAGCAGACTGCTC
Gene
        : LAGE1
Segment# : 6
Offset
       : 76
1st Codon : 1
 G R C P C G A R R P D S R L L Q L H I T M P F S S P M E A E
GGCAGATGCCCTTGCGGAGCCAGAAGGCCTGACTCCAGGCTCCTGCAACTGCATATCACAATGCCTTTCTCCAGCCCTATGGAAGCCGAA
Gene
Segment# : 7
Offset
       : 91
1st Codon : 1
 Q L H I T M P F S S P M B A B L V R R I L S R D A A P L P R
CAGCTCCACATTACCATGCCCCTTTAGCTCCCCCATGGAGGCTGAGGAGGATTCTGTCCAGGGATGCCGCTCCCCCAGA
        : LAGE1
Gene
Segment# : 8
Offset
       : 106
1st Codon : 1
 L V R R I L S R D A A P L P R P G A V L K D P T V S G N L L
CTGGTCAGGAGAATCCTCAGCAGAGACGCTGCCCCTCTGCCTAGGCCTGGCGCTGTGCTCAAGGATTTCACAGTGTCCGGCAATCTGCTC
        : LAGE1
Segment# : 9
Offset
       : 121
1st Codon : 1
PGAVLKDFT V S G N L L F I R L T A A D H R Q L Q L S
CCCGGAGCCGTCCTGAAAGACTTTACCGTCAGCGGAAACCTCCTGTTTATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCC
Gene
       : LAGE1
Segment# : 10
Offset
       : 136
1st Codon: 1
FIRLTAADHRQLQLSISSCLQQLSLLMWIT
TTCATTAGGCTCACCGCTGCCGATCACAGACAGCTCCAGCTCAGCATTAGCTCCTGCCTCCAGCAACTGTCCCTGCTCATGTGGATCACA
Gene
Segment# : 11
Offset
       : 151
1st Codon: 1
ISSCLQQLSLLMWITQCFLPVFLAQAPSGQ
Gene
Segment# : 12
Offset
       : 166
1st Codon : 1
Q C P L P V P L A Q A P S G Q R R A A
```

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CAGTGTTTCCTCCCCGTCTTCCTCGCCCAAGCCCCTAGCGGACAGAGAAGGGCTGCC

Segments in scrambled order:

MAGE-1 #15

A P B B B I W B B L S V M B V Y D G R B H S A Y G B P R K L GCCCCTGAGGAAGAGATTTGGGAAGACTCAGGAAGGTGTATGACGGAAGGGAACACTCCGCCTTATGGCGAACACCCAGAAAGCTC

MAGE-1 #4

PRAME #10

T V W S G N R A S L Y S F P E P E A A Q P M T K K R K V D G ACCOTCTGGTCCGGCAATAGGGCTAGCCTCACTCCTTCCCTGAGGCTGGCCCCAACCCCATGACCAAAAAGAGAAAGGTCGACGGA

MAGE-3 #14

Q I M P K A G L L I I V L A I I A R E G D C A P E E K I W E CAGATTATGCCTAAGGCTGGCCTCCTGATTATCGTCCTGGCTATCATTGCCAGAGAGGGGGGAGACTGTGCCCCTGAGGAAAAGATTTGGGAA

PRAME #9

PRAME #8

L D V L L A Q E V R P R R W K L Q V L D L R K N S H Q D F W CTGGATGTGCTCCTGGCTCCAGGAGTGGAAGCTCCAGGAGTTCTGG

NYNSOLD #2

PRAME #24

Q S P S V S Q L S V L S L S G V M L T D V S P E P L Q A L L CAGTCCCCTCCGGCTCCAGCCTCTCCCGGCTCATCCTCCCGGCTCACCCTCCCGACCCCTCCAGGCTCTGCTC

MAGE-1 #17

MAGE-1 #6

R Q P S E G S S R E E E G P S T S C I L E S L F R A V I T AGGCAACCCTCCGGAGGGAAGGCCGCTCATCACA

Bage #1

PRAME #34

T F Y D P E P I L C P C F M P N A A ACCTITIACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCAATGCCGCT

MAGE-3 #12

I B L M E V D P I G H L Y I F A T C L G L S Y D G L L G D N ATCGAACTGATGGAGGGCGACCACTTTCGAACATTTTCGCTACCTGTCTGGGACTGTCCTACGATGGCCTCCTGGGAGACAAT

GAGE-1 #2

TRP2IN2 #2

E A G G F F P W L K V Y Y Y R F V I G L R V W Q W E V I S C GAGGCTGGCGGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTGTGATTGGCCTCAGGGTCTGGCAATGGGAAGTGATTAGCTGT

PRAME #1

A A M E R R R L W G S I Q S R Y I S M S V W T S P R R L V E GCCGCTATGGAAAGGAGGAGGCTCCGGGAAGGCTCCAGGAAGGCTCCTGGAA

TRP2IN2 #1

A A L M B T H L S S K R Y T B E A G G P F P W L K V Y Y Y R GCCGCTCTGATGGAGACACCTCCAAGAGATACACAGAGGAAGCCGGAGGCTTTTTCCCTTGGCTCAAGGTCTACTATTACAGA

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MAGE-1 #1

A A M S L E Q R S L H C K P E E A L E A Q Q E A L G L V C V GCCGCTATGTCCCTGGAACAGAGAGCCTCCACTGTAAGCCTGAGGAAGCCCTCGAGGCTCAGCAAGAGGCTCTGGGACTGGTCTGCGTC

MAGE-1 #3

Q A A T S S S S P L V L G T L B E V P T A G S T D P P Q S P CAGGCTGCCACAAGCTCCCCCTCGTGCTCGCACACGCTCCCCACAGGCTCCCCACAGCCCTCCCCAAAGCCCT

PRAME #4

A L E L L P R E L F P P L F M A A F D G R H S Q T L K A M V GCCCTCGAGCTCTGCCTAGGGAACCCTCTGTTTATGGCTGCCTTTGACGGAAGGCATAGCCAAACCCTCAAGGCTATGGTC

MAGE-3 #16

E L S V L E V P E G R E D S I L G D P K K L L T Q H F V Q E GAGCTCAGCGTCCTGGAAGTGTTTTGGGGGAAGGGGAAGCTCCATCCTCGGCGATCCCAAAAGGCTCCTGACACAGCATTTCGTCCAGGAA

MAGE-1 #11

ESLQLVFGIDVKEADPTGHSYVLVTCLGGLGGCTGCCCTGCCTCCTGCTCCTGCTCCTGCGCACTCTCTGGGACTGTCCC

MAGE-3 #5

PDPPQSPQGASSLPTTMNYPLWSQSYEDSSCCCGATCCCCCTCAGTCCCCCCCAAGGCGCTAGCTCCCTGCCACAATGAATTACCCTCTGTGGAGCCAAAGCTATGAGGATAGCTCC

LAGE1 #1

NYNSOla #12

Q C F L P V F L A Q P P S G Q R R A A CAGTGTTTCCTCCCCGTCTTCCTCGCCCAACCCCCTAGCGGACAGAGAAGGGCTGCC

gp100In4 #2

T W G B G L P S Q P I I H T C V Y F F L P D H L S P G R P F ACCTGGGGCGAAGGCCTCCCCCAGCCTATCATTCACACATGCGTCTACTTTTTCCTCCCCGATCACCTCAGCTTTGGCAGACCCTTT

MAGE-1 #7

S T S C I L B S L F R A V I T K K V A D L V G F L L L K Y R AGCACAAGCTGTATCCTCGAGTCCCTGTTTTAGGGCTGTGATTACCAAAAAGGTCGCCGATCTGGTCGGCTTTCTGCTCCTGAAATACAGA

NYNSOla #1

GAGE-1 #7

D G P D G Q E M D P P N P E E V K T P E E B M R S H Y V A Q GACGGACCCGAAGAGGCCAAGAGGCCATTACGTCGCCCAA

NYNS01a #11

ISSCLQQLSLLMWITQCFLPVFLAQPPSGQATCTCCCAGCTGTCTCTGCCTGGCTCAGCCTCCCTCCGGCCAA

PRAME #26

MAGE-3 #17

L G D P K K L L T Q H P V Q E N Y L B Y R Q V P G S D P A C CTGGGAGACCTTAGAAACTGCTCACCAACACTTTTGGCAAGAGAATTACCTCGAGTATAGGCAAGTGCCTGGCTCCGACCTGCTGT

MAGE-1 #

E A L E A Q Q E A L G L V C V Q A A T S S S P L V L G T L GAGGCTCTGGAAGCCCTAGGAAGCCCTCTGGGAAGCCCTCTGGGAAGCCCTCTGGGAAGCCCTCTGGGAAGCCCTC

NYNSO1a #7

E F Y L A M P F A T P M E A E L A R R S L A Q D A P P L P V GAGTTTTACCTCGCCATGCCCATGCCCATGCACCCATGGAGGCTCGCCAGAAGGTCCCTGGCTCAGGATGCCCCTCCCCTCCCCGTC

NVNCOIL #4

B B A P R G V R M A A R L Q G A A GAGGAAGCCCCTAGGGGGATGAGAATGGCTGCCAGACTGCAAGGCGCTGCC

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BAGE #3

W R L B P B D G T A L C F I F A A TGGGGACCGGAACCGGAACCGGAACCGCTCTGTGTTTCATTTTCGCTGCC

GAGR-1 #3

E Q F S D E V E P A T P E E G E P A T Q R Q D P A A A Q E G GAGCAATTCTCCGACGAAGTGGAACCCCCTACCCCTACGGAAGGGGAACCCCGCTACCCCAAGAGGGAA

MAGE-3 #6

T M N Y P L W S Q S Y E D S S N Q E E E G P S T F P D L E S ACCATGAACTATCCCCTCTGGTCCCAGTCCTAGGAAGACTCCAGGAAGAGGAAGGGCCCTAGGACATTCCCTGACCTCGAGTCC

MAGE-3 #

NQEEEGPSTFPDLESEFQAALSRKVAELVH AACCAAGAGGGAAGAGGGACCCTCCACCTTTCCCGATCTGGAAAGCGAAATTCCAAGCCGCTCTGTCCAGGAAAGTGGCTGAGCTCGTGCAT

PRAME #1:

V D L F L K B G A C D B L F S Y L I B K V K R K K N V L R L GTGGATCTGTTCTGAAGAGGGAGAGGCTGTGAGACTGTTTAGCTAGTTGAGAAAGTGAAAAGGAAAAGAATGTGCTCAGGCTC

NYNSO1a #10

MAGR-3 #1

A A M P L B Q R S Q H C K P B B G L B A R G B A L G L V G A GCCCTATGCCTCTGGACAGGAGGCCACACTGTAGCCTGAGGAGGCCTCTGGGGGGAGGCCTCTGGGAGGCTCTGGGACTGGTCGGCGCT

NYNSOla #2

D A D G P G G P G I P D G P G G N A G G P G B A G A T G G R GACECTGACGGAGGCCCTGGCGATTCCCGATGCCCTGGCGGAAACGCTGGCGGACCCGGAGAGGCTGCGCTGCCGAGAGGCAGA

MAGR-3 #19

Y B F L N G P R A L V B T S Y V K V L H H M V K I S G G P H TACGAATTCCTCTGGGGGACCCCGTGGAAACCTCCTACGTCAAGGTCCTGCATCACATGGTGAAAATCTCCGGCGGACCCCAT

PRAME #23

ITNCRLSEGDVMHLSQSPSVSQLSVLSLSG ATCACAAACTGTAGGCTCAGCGAAGGCGTCAGCCTAGCGTCAGCCTCAGCCTCAGCGCGA

MAGR-3 #18

N Y L E Y R Q V P G S D P A C Y E F L W G P R A L V E T S Y AACTATCTGGAATACAGACAGGTCCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCTAGGGCTCTGGTCGAGACAAGCTAT

MAGE-3 #11

VIPSKASSSLQLVFGIELMBVDPIGHLYIPGTGATTTTTTTCCCAAGGCTAGCTCCAGCTCCAGCTCGTGTTTGGCATTGAGCTCATGGAAGTGGATCCCATTGGCCATCTGTATATCTTT

PRAME #21

PRAME #20

Y I A Q F T S Q F L S L Q C L Q A L Y V D S L F F L R G R L TACATTGCCCAATTCACAAGCCAATTCCTCAGGCGAAGGCTC

PRAME #7

GQHLHLBTFKAVLDGLDVLLAQBVRPRRWK

TACP1 #10

FIRLT A A D H R Q L Q L S I S S C L Q Q L S L L M W I T TTCATTAGGCTCACCGCTGCCGATCACAGACAGCTCCAGCTCAGCATCACGACTCCAGCAACTGTCCTGCTCATGTGGATCACA

PRAME #15

C C K K L K I P A M P M Q D I K M I L K M V Q L D S I B D L
TGCTGTAAGAAACTGAAAATGTTTGCCATGCCATGCAGGATATCAAAATGATTCTGAAAATGGTCCAGCTCGACTCCATCGAAGACTC

NYNSOla #5

GAPRGPHGGAASGLNGCCRCGARGGGGCCCGAAAGCACTGCTCCCAGAGGCCCTCACGGAGGCCCTCCACGGCTCAACGGATGCTGTAGGTGTGGCGCTAGGGGACCCGAAAGCAGACTGCTC

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MAGE-1 #8

K K \dot{V} A D L \dot{V} G \dot{F} L L K \dot{Y} R A R B \dot{P} V T K A B M L B S V I AAGAAAGTGGCTGACCTCGTGGGATTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGAGTCCGTGATT

MAGE-1 #13

PRAME #2

S I S A L Q S L L Q H L I G L S N L T H V L Y P V P L B S Y AGCATTAGGGCTCTGCAAAGCCTCATCGGACACCTCATCGGCTCTGCACCTCATCGGCTCTGCCATGTGCTCTTGCCTCTGGAAAGCTAT

MAGE-3 #15

I A R E G D C A P E E K I W E E L S V L E V F E G R E D S I ATCCCTAGGGAAGGCGATGCCCTCCCGAAGAGAAATCTGGGAGGAACTGTCCGTGCTCGAGGGTCTTCGAAGGCAGAGGATAGCATT

PRAME #22

D Q L L R H V M N P L B T L S I T N C R L S B G D V M H L S GACCAACTGCTCAGGCATGTGATGAACCCTCTGGAAACCCTCAGCATTACCAATTGCAGACTGTCCGAGGGAGACGTCATGCATCTGTCC

MAGE-1 #19

PRAME #30

S N L T H V L Y P V P L E S Y E D I H G T L H L E R L A Y L AGCAATCTGACACACGTCCTGTATCCCGTCCCCCTCGAGGCTTACCTC

NYNSO1b #1

A A M L M A Q E A L A F L M A Q G A M L A A Q E R R V P R A GCCGCTATGCTCATGGCTCAGGAAGGAGCCCTTCTGATGGCCCAAGGCGCTTATGCTCGCCGCTCAGGAAAGGAGAGTGCCTAGGGCT

MAGE-1 #10

K N Y K H C F P B I F G K A S B S L Q L V F G I D V K B A D AAGAATTACAAACACTGTTTCCCTGAGATTTTCGGAAAGGCTGGGAAGCCTCCAGCTGTTTTGGCATTGACGTCAAGGAAGCCGAT

MAGE-3 #4

T L V E V T L G E V P A A E S P D P P Q S P Q G A S S L P T ACCOTCGTGGAAGTGACACTGGGAAGGCCTCAGGGAGCCTCCCGAAAGCCCTCAGGGAGCCTCCAGGCAGCCTCCCCACA

PRAME #32

HARLRBLLCELGRPSMVWLSANPCPHCGDR CACGCTAGGCTCAGGGAACTGCGAACTGGGAAGGCCTAGCATGCTGTGCCCATTCCGGAGACAGA

PRAME #25

V M L T D V S P E P L Q A L L E R A S A T L Q D L V F D E C GTGATGCTGACAGACGTCAGGCCTTGGAGGCCTTCGGAGGGCTTAGGCCTACCCTCCAGGATCTGGTCTTCGATGAGTGT

GAGE-1 #

BDBGASAGGAGCCTCCGCCGGACAGGGACCCAAACCCGAAGCCCAAGCCAAGAGCAAGGCCATCCCCAAACCGGATGCGAA

MAGE-3 #10

E M L G S V V G N W Q Y P P P V I P S K A S S S L Q L V P G GAGATGCTGGGAAGCGTCGTGGGAAACTGGTCTTCCGGAAGCCTCCAGCTCCTGCAACTGGTCTTCGGA

GAGE-1 #1

A M S W R G R S T Y R P R P R R Y V E P P B M I G P M R P GCCGCTATGTCCTGGGAGGCAGAGGCACATACAGACCCAGAGGCTATGTGGAACCCCTGAGATGATGAGGCCTATGAGGCCT

PRAME #2

Y I S M S V W T S P R R L V E L A G Q S L L K D E A L A I A
TACATTAGCATGAGCATCTGGACAAGCCCTAGGAGACTGGTCGAGGCTCCTGGCTATCGCT

MAGE-1 #16

Y D G R E H S A Y G E P R K L L T Q D L V Q E K Y L E Y R Q
TACGATGGCAGAGAGCATAGCGCTTACGGAGAGCCTAGGAAACTGCTCACCCAAGACCTCGTGCAAGAGAAATACCTCGAGTATAGGCAA

LAGB1 #12

Q C F L P V F L A Q A P S G Q R R A A CAGTGTTTCCTCCCCGTCTTCCTCGCCCAAGCCCCTAGCGGACAGAGAAGGGCTGCC

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MAGE-3 #20

V K V L H H M V K I S G G P H I S Y P P L H E W V L R E G E GTGAAAGTGCTCCACCATATGGTCAAGATTAGCGGAGGCCCTCACCATTAGCTGTCCCCCTCTGCATGAGTGGGTGCTCAGGGAAGGCGAA

LAGE1 #7

Q L H I T M P F S S P M E A B L V R R I L S R D A A P L P R CAGCTCCACATTACCATGCCCTTTAGCTCCCCATGGAGGCTGAGCTCGTGAGAAGGATTCTGTCCAGGGATGCCGCTCCCCCAGA

WWNSO1a #9

PGVLLKEPTVSGNILTIRLTAADHRQLQLSCCCGGAGAGCTCACCGGAGAGCTCACCGCAGACGCGCAACCATCCGCAACCATCAGACCGCAGCCGCTGACCATAGGCAACTGCCACTGCCC

PRAME #16

K M I L K M V Q L D S I E D L E V T C T W K L P T L A K P S AAGATGATCCTCAAGATGGCAACTGCATAGCATTGAGATCTCCCAAATTCTCC

MAGE-1 #14

F L I I V L V M I A M E G G H A P E E E I W E E L S V M E V
TTCCTCATCATCTGTGATGATGATGGTGGTGGGGGGACTCCCGTGATGGAGGGGACTCTCCGTGATGGAGGGGACTCTCCGTGATGGAGGGTC

PRAME #17

EVTCTWKLPTLAKFSPYLGQMINLRRLLLSGAGGTCACCTGGCAAATGATTAACCTCAGGAGACTGCTCCTGTCC

MAGR-3 #:

EGLEARGEA AGCCTCGGCCTCGGGGGGCCCAAGCCCCTGCCACAGAGGAACAGGAAGCCGCTAGCTCCAGCTCC

MAGE-3 #21

PRAME #19

H I H A S S Y I S P E K E E Q Y I A Q F T S Q F L S L Q C L CACATTCACGCTAGCTCCCAGTATGCCCTCGGAAAGAGGAACAGTATATCGCTCAGTTTACCTCCCAGTTTCTGTCCCTGCAATGCCTC

NYNSOla #3

GNAGGPGBAGATGCGGAGCCACAGGCGGAGGGGGACCCAGAGGCCTGGCGCTGCCAGAGCCTCGGCCCTGGCGAG

NYNSOla #4

MAGE-1 #5

NYNSOla #8

LARRSLAQDAPPLPVPGVLLKEFTVSGNILCTGGCTAGGAGAAGCCTCCCCCAAGACGCTCCCCCTCTGCCTGGCGTCCTGCTCAAGAGAATTCACAGTGTCCGGCAATATCCTC

PRAME #5

A A P D G R H S Q T L K A M V Q A W P F T C L P L G V L M K GCCGCTTTCGATGCAGACACTCCAGACACTCAAAGCCATGGTGCAAGCCTTTACCTGTCTGCCTCTGCGAGTGCTCATGAAA

MAGE-1 #20

IKVSARVRFFFPSLREAALREBBBGVAA

PRAME #27

G I T D D Q L L A L L P S L S H C S Q L T T L S F Y G N S I GGCATTACCGATGACCAACTGCTCGCCTCCTGCCTAGCCTCAGCCATTGCTCCCAGCTCACCACACTGTCCTTCTATGGCAATAGCATT

GAGE-1 #8

V K T P B B B M R S H Y V A Q T G I L W L L M N N C F L N L GTGAAAACCCCTGAGGAAGAGATGAGGTCCCACTATGTGGCTCAGACAGGCATTCTGTGGCTGATGAATAACTGTTTCCTCAACCTC

LAGRI #11

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PRAME #14

Y L I'E K V K R K K N V L R L C C K K L K I F A M P M Q D I
TACCTCATCGAAAAGGTCAAGAGAAAAGAAAAACGTCCTGAGACTGTGTTGCAAAAAGGTCAAGATTTTCGCTATGCCTATGCAAGACATT

MAGE-1 #9

A R E P V T K A E M L E S V I K N Y K H C F P E I P G K A S GCCAGAGAGCCTGTGACAAAGGCTGGAGAGCCTCATCAAAAACTATAAGCATTGCTTTCCCGAAATCTTTGGCAAAGCCTCC

Lagel #8

LVRRILSRDAAPLPRPGAVLKDFTVSGNLLCTGGTCAGGAGAATCCTCAGGAGAATCCTCAGGAGAATCCTCAGGAGAATCCTCAGGCTGCCCAATCTGCTC

PRAME #21

H C S Q L T T L S F Y G N S I S I S A L Q S L L Q H L I G L CACTGTAGCCAACTGACAACCCTCAGCTTTTACGGAAACTCCATCTCCATCTCCGCCCTCCAGCTCCTGCTCCAGCATCTGATTGGCCTC

PRAME #33

M V W L S A N P C P H C G D R T F Y D P B P I L C P C F M P ATGGTCTGGCCTAACCCTTGCCCTCACTGGCGATAGGACATTCTATGACCCTGAGCCTATCCTCTGCCCTTGCCTTTATGCCT

gp100In4 #1

A A S W S Q K R S F V Y V W K T W G B G L P S Q P I I H T C GCCGCTAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGAAGGGACTGCCTAGCCAACCCATTATCCATACCTGT

BAGE #2

gp100In4 #3

V Y F F L P D H L S F G R P F H L N F C D F L A A GTGTATTTCTTTCTGCCTGCCCTGCCTTCCGCAAGCCCTTTCCATCTGAATTTCTGTGACTTTCTGGCTGCC

PRAME #18

MAGE-3 #3

PRAME #6

Q A W P F T C L P L G V L M K G Q H L H L E T P K A V L D G CAGGCTTGGCCTTCCCCCTCGGCGTCCTGATGAAGGGACAGCATCTGCAACCTTTAAGGCTGTGCTCGACGGA

PRAME #12

NYNSO1b #3

A E V P G A Q G Q Q G P R G R E E A P R G V R M A A R L Q G GCCGAAGTGCCTGGGGCTCAGGGCAGGCCTCAGGGGAAGGGCAAGGCCTCCAGGGAAGAGGCTCCCAGAGGCGTCAGGATGCCCGCTAGGCTCCAGGGA

LAGB1 #5

G A P R G P H G G A A S A Q D G R C P C G A R R P D S R L L GGCGCTCCCAGAGGCCCTCACGGAGGCCCTCCCCCCAAGACGGAAGGTGTCCCTGTGGCGCTAGGAGACCCGATAGCAGACTGCTC

LAGE1 #4

G P R G A G A A R A S G P R G G A P R G P H G G A A S A Q D GGCCCTAGGGGAGCCGCTAGGGCTAGGGCTAGGGCTCAGGGCCCCCTAGGGGACCCCCATGGCGAGCCGCTAGGGCTCAGGAT

DDRWD #3

LAGQSLLKDEALAIAALELLPRELPPLFM CTGGCTGGCCAAAGCCTCTGAAAGACCCTCTCGCCATTGCCGCTCTGGAACTGCTCCCCAGAGAGCTCTTCCCCCCCTCTTCATG

GAGE-1 #4

PRAME #11

PEAAQPMTKKRKVDGLSTEAEQPFIPVEVL

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LAGE1 #6

G R C P C G A R R P D S R L L Q L H I T M P F S S P M E A E GGCAGATGCCCTTGCGGAGCCAGAAGGCCTGACTCCAGGCTCCTGCAACTGCATATCACAATGCCTTTCTCCAGCCCTATGGAAGCCGAA

P G A V L K D F T V S G N L L F I R L T A A D H R O L O L S CCCGGAGCCGTCCTGAAAGACTTTACCGTCAGCGGAAACCTCCTGTTTATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCC

PRAME #31

EDIHGTLHLERLAYLHARLRELLCELGRPS GAGGATATCCATGGCACACTGCATCTGGAAAGGCTCGCCTATCTGCATGCCAGACTGAGAGAGCTCCTGTGTGAGCTCGGCAGACCCTCC

D S Q E Q G H P Q T G C E C E D G P D G Q E M D P P N P E E GACTCCCAGGAACAGGGACACCCTCAGACAGGCTGTGAGTGTGAGGATGGCCCTGACGGACAGGAAATGGATCCCCCTAACCCTGAGGAA

F V I G L R V W Q W E V I S C K L I K R A T T R Q P A A TTCGTCATCGGACTGAGAGTGTGGCAGTGGGAGGTCATCTCCTGCAAACTGATTAAGAGAGCCCACAACCAGACAGCCTGCCGCT

D A D G P G G P G I P D G P G G N A G G P G B A G A T G G R GACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGACCCGGAGAGGCTGGCGCTACCGGAGGCAGA

PTGHSYVLVTCLGLSYDGLLGDNQIMPKTG CCCACAGGCCATAGCTATGTGCTCGTGACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAACCAAATCATGCCCAAAACCGGA

P L L L K Y R A R E P V T K A E M L G S V V G N W Q Y F P P

T G I L W L L M N N C F L N L S P R K P A A ACCGGAATCCTCTGGCTCCTGATGAACAATTGCTTTCTGAATCTGTCCCCCAGAAAGCCTGCCGCT

MAGE-3 #8

E F Q A A L S R K V A E L V H F L L K Y R A R B P V T K A GAGTTTCAGGCTGCCCTCAGCAGAAAGGTCGCCGAACTGGTCCACTTTCTGCTCCTGAAATACAGAGCCAGAGAGCCTGTGACAAAGGCT

V P D S D P A R Y E F L W G P R A L A B T S Y V K V L E Y V GTGCCTGACTCCGACCCTGCCAGATACGAATTCCTCTGGGGACCCAGAGCCCTCGCGAAACCTCCTACGTCAAGGTCCTGGAATACGTC

NYNSOla #6

G C C R C G A R G P E S R L L B P Y L A M P P A T P M E A E GGCTGTTGCAGATGCGGAGCCAGAGGCCCTGAGTCCAGGCTCCTGGAATTCTATCTGGCTATGCCTTTCGCTACCCCTATGGAAGCCGAA

A T C L G L S Y D G L L G D N Q I M P K A G L L I I V L A I GCCACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAACCAAATCATGCCCCAAAGCCGGACTGCTCATCATTGTGCTCGCCATT

G N A G G P G B A G A T G G R G P R G A G A A R A S G P R G GGCAATGCCGGAGGCCCTGGCGAAGCCGGAGCCACAGGCGGAAGGGGGACCCAGAGGCGTGCCAGAGCCTCCGGCCCTAGGGGA

Artificial Protein:

APBEBIWERLSVMEVYDGREHSAYGBPRKLEEVPTAGSTDPPQSPQGASAFPTTINFTRQTVWSGNRASLYSPPEPBAAQPMTKKRKVDGOIMPKAGL LIIVLAIIAREGDCAPBEKIWELQVLDLRKNSHQDFWTVWSGNRASLYSFPELDVLLAQEVRPRRWKLQVLDLRKNSHQDFWQGAMLAAQERRVPRAA evpgaogoogprgrospsvsqlsvlslsgvmltdvspeplqallltqdlvqekyleyrqvpdsdparyeplmgprqpsegsssreeegpstscilesl FRAVITAAMAARAVPLALSAQLLQARLMKBESPVVSTPYDPEPILCPCFMPNAAIELMEVDPIGHLYIFATCIGLSYDGLLGDNRRYVEPPEMIGPMR PEQFSDEVEPATPEEGBAGGFFPPWLKVYYYRPVIGLRVWQWEVISCAAMERRRLMGSIQSRYISMSVWTSPRRLVEAALMETHLSSKRYTEEAGGFFP WLKVYYYRAMSLEQRSLHCKPEEALEAQQEALGLVCVQAATSSSSPLVLGTLEEVPTAGSTDPPOSPALELLPRELFPPLFMAAFDGRHSOTLKAMV ELSVLEVFEGREDSILGDPKKLLTQHFVQEESLQLVFGIDVKEADPTGHSYVLVTCLGLSPDPPQSPQGASSLPTTMNYPLWSQSYEDSSAAMQAEGQ GTGGSTGDADGPGGPGIPDGPGQCFLPVFLAQPPSGQRRAATWGEGLPSQPIIHTCVYFFLPDHLSFGRPFSTSCILESLFRAVITKKVADLVGFLLL KYRAAMQABGRGTGGSTGDADGPGGPGIPDGPGDGPDGQEMDPPNPEEVKTPEEEMRSHYVAQISSCIQQLSLIMWITQCFLPVFLAQPPSGQERASA TLQDLVFDBCGITDDQLLALLPSLSLGDPKKLLTQHPVQENYLEYRQVPGSDPACEALBAQQEALGLVCVQAATSSSSPLVLGTLEFYLAMPFATPME AKLARRSLAQDAPPLPVBEAPRGVRMAARLQGAAWRLEPEDGTALCP1FAAEQFSDEVEPATPEBGEPATQRQDPAAAQBGTMYPLWSQSYEDSSNQ EEEGPSTPPDLESNQEEEGPSTPPDLESEFQAALSRKVAELVHVDLFLKEGACDELPSYLIEKVKRKKNVLRLTIRLTAADHRQLQLSISSCLOOLSL LMWITAAMPLEQRSQHCKPEEGLBARGEALGLVGADADGPGGPGIPDGPGGNAGGPGEAGATGGRYEFLWGPRALVETSYVKVLHHMVKISGGPHITN CRLSEGDVMHLSQSPSVSQLSVLSLSGNYLEYRQVPGSDPACYEPLWGPRALVETSYVIFSKASSSLQLVPGIEIMEVDPIGHLYIPQALYVDSLPFL

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 ${\tt RGRLDQLLRHVMNPLETLSYLAQFTSQFLSLQCLQALYVDSLPFLRGRLGQHLHLETFKAVLDGLDVLLAQEVRPRRWKFIRLTAADHRQLQLSISSC$ LQQLSLLMNITCCKKLKIFAMPMQDIKMILKMVQLDSIEDLGAPRGPHGGAASGLNGCCRCGARGPESRLLKKVADLVGFLLLKYRAREPVTKAEMLE sviydgllgdnqimpktgfliivlvmiamegghsisalqsllqhliglsnlthvlypvplesyiaregdcapeekiweelsvlevfegredsidqllr hvmnpletlsitncrlsegdvmhlsralabtsyvkvleyvikvsarvrfffpslrsnlthvlypvplesyedihgtlhlerlaylaamlmaqealafl Maqgamlaaqerrvpraknykhcppeipgkaseslqlvpgidvkbadtlvbvtlgbvpaabspdppqspqgasslptharlrellcblgrpsmvmlsa npcphcgdrvmltdvspeplqallerasatlqdlvfdecedegasagqgpkpeadsqeqghpqtgceceemlgsvvgnwqyffpv1fskassslqlvf gaamswrgrstyrprprryveppemigpmrpyismsvwtsprrlvelagqsilkdealaiaydgrehsaygeprklltqdlvqekylbyrqqcflfvf LAQAPSGQRRAAVKVLHHMVKISGGPHISYPPLHEWVLREGEQLHITMPPSSPMEAELVRRILSRDAAPLPRPGVLLKEFTVSGNILTIRLTAADHRQ LQLSKMILKMVQLDSIEDLEVTCTWKLPTLAKPSFLIIVLVMIAMEGGHAPEBEIWEELSVMEVEVTCTWKLPTLAKFSPYLGQMINLRRLLLSEGLE argealglygaqapateeqbaassssisypplhewvlregebaahihassyispekbeqyiaqptsqplslqclgnaggpgeagatggrgprgagaar asgpccgprgagaarasgpccgaprgphcgaasglnqgasappttinftrqrqpsecssreeegplarrslaqdapplpvpgvllkeptvsgnilaa pdgrhsqtlkamvqawpftclplgvlmkikvsarvrfpppslrbaalreebegvaagitddqllallpslshcsqlttlsfygnsivktpbbemrshy vaqtgilwlimncpinlissclqqlslimwitqcflpvplaqapsgqyliekvkrkknvlrlcckklkipampmqdiarepvtkaemlesviknykh CFPBIFGKASLVRRILSRDAAPLPRPGAVLKDFTVSGNLLHCSQLTTLSFYGNSISISALQSLLQHLIGLMVWLSANPCPHCGDRTFYDPEPILCPCF mpaasmsqkrsfvyvwktmgeglpsqpiihtcllqarlmkbespvvswrlbpedgtalcfifvyfflpdhlsfgrpfhlmpcdflaapylgqminlrr LLLSHIHASSYISPEKEEQQAPATEEQEAASSSSTLVEVTLGEVPAAESQAWPFTCLPLGVLMKGQHLHLETPKAVLDGLSTEAEQPFIPVEVLVDLF ${\tt LKEGACDELPSAEVPGAQGQQGPRGREEAPRGVRMAARLQGGAPRGPHGGAASAQDGRCPCGARRPDSRLLGPRGAGARASGPRGGAPRGPHGGAAS}$ aqdlagqsllkdeala1aalellprelppplfmepatqrqdpaaqegedegasagqgpkpeapeaaqpmtkkrkvdglstbaeqpf1pvevlgrcpc GARRPDSRLLQLHITMPFSSPMEAEPGAVLKDFTVSGNLLFIRLTAADHRQLQLSEDIHGTLHLERLAYLHARLRELLCELGRPSDSQEQGHPQTGCE CEDGPDGQEMDPPNPEEFVIGLRVWQWEVISCKLIKRATTRQPAADADGPGGPGIPDGPGGNAGGPGEAGATGGRPTGHSYVLVTCLGLSYDGLLGDN QIMPKTGPLLLKYRAREPVTKABMLGSVVGNWQYFFPTGILWLLMNNCPLNLSPRKPAABPQAALSRKVABLVHFLLLKYRAREPVTKAVPDSDPARY eplwgpralaetsyvkvlbyvgccrcgargpbsrllefylamppatpwrabatclglsydgllgdnqimpkaglliivlaignaggpgbagatggrgp RGAGAARASGPRG

Artificial DNA:

GCCCCTGAGGAAGAGTTTGGGAAGAGCTCAGCGTCATGGAAGTGTATGACGGAAGGGAACACTCCGCCTATGGCGAACCCCAGAAAGCTCGAGGAAGT ATAGGGCTAGCCTCTACTCCTTCCCTGAGCCTGAGGCTGCCCAACCCATGACCAAAAAGAGAAGATCGACGGACAGATTATGCCTAAGGCTGGCCTC CTGATTATCGTCCTGGCTATCATTGCCAGAGAGGGGAGACTGTGCCCCTGAGGAAAAGATTTGGGAACTGCAAGTGCTCGACCTCAGGAAAAACTCCCA CCAAGACTTTTGGACAGTGTGGAGCGGAAACAGAGCCTCCCTGTATAGCTTTCCCGAACTGGATGTGCTCCTGGCTCAGGAAGTGAGACCCAGAAGGT GAGGTCCCCGGAGCCCAAGGGCCAACAGGGACCCAGAGGCAGACAGTCCCCCTCCGTGTCCCAGCTCAGCGTCCTGTCCCTGTCCCGGCGTCATGCTCAC CGTCGTGTCCACCTTTTACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCAATGCCGCTATCGAACTGATGGGGGTCGACCCTATCGGACACC TCTACATTTTCGCTACCTGTCTGGGACTGTCCTACGATGGCCTCCTGGGAGACAATAGGAGATACGTCGAGCCTCCCGAAATGATTGGCCCTATGAGA CCCGAACAGTTTAGCGATGAGGTCGAGCCTGCCACACCCGAAGAGGGGAGGGCTGGCGGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTGT GATTGGCCTCAGGGTCTGGCAATGGGAAGTGATTAGCTGTGCCGCTATGGAAAGGAGAAGGCTCTGGGGAAGCATTCAGTCCAGGTATATCTCCATGT CCGTGTGGACCTCCCCAGAAGGCTCGTGGAAGCCGCTCTGATGGAGACACACCTCAGCTCCAAGAGATACACAGAGGAAGCCGGAGGCTTTTTCCCT TGGCTCAAGGTCTACTATTACAGAGCCGCTATGTCCCTGGAACAGGAGAAGCCTCCACTGTAAGCCTGAGGAAGCCCTCGAGGAGGCTCAGCAAGAGGCTCT GGACTGGTCTGCGTCCAGGCTGCCACAAGCTCCAGCTCCCCCCTCGTGCTCGGCACACTGGAAGAGGTCCCCACAGCCGGAAGCACAGACCCTCCCC AAAGCCCTGCCCTCGAGCTCCTGCCTAGGGAACTGTTTCCCCCTCTGTTTATGGCTGCCTTTGACGGAAGGCATAGCCAAACCCTCAAGGCTATGGTC GAGCTCAGCGTCCTGGAAGTGTTTGAGGGAAGGGGAAGACTCCATCCTCGGCGATCCCAAAAAGCTCCTGACACAGCATTTCGTCCAGGAAGAGTCCCT GCAACTGGTCTTCGGAATCGATGTGAAAGAGGCTGACCCTACCGGACACTCCTACGTCCTGGTCACCTGTCTGGGACTGTCCCCCGATCCCCCTCAGT CCCCCAAGGCGCTAGCTCCCTGCCTACCACAATGAATTACCCTCTGTGGAGCCAAAGCTATGAGGATAGCTCCGCCGCTATGCAAGCCCAAGGCCAA GGCACAGGCGGAAGCACAGGCGATGCCGATGGCCCTGGCGGACCCGGAATCCCTGACGGACCCGGACAGTGTTTCCTCCCCGTCTTCCTCGCCCAACC CCCTAGCGGACAGAGAGGGCTGCCACCTGGGGCGAAGGCCTCCCCTCCCAGCCTATCATTCACACATGCGTCTACTTTTTCCTCCCCGATCACCTCA GCTTTGGCAGACCCTTTAGCACAAGCTGTATCCTCGAGTCCCTGTTTAGGGCTGTGATTACCAAAAAGGTCGCCGATCTGGTCGGCTTTCTGCTCCTG AAATACAGAGCCGCTATGCAAGCCGAAGGCAGAGGCACAGGCGGAAGCACAGGCGATGCCGATGCCGTTATGCAGGACCCGGAATCCCTGACGGACCCGG AGACGGACCCGATGGCCAAGAGATGGACCCTCCCAATCCCGAAGAGGTCAAGACACCCGAAGAGGGAAATGAGAAGCCATTACGTCGCCCAAATCTCCA ACACTGCAAGACCTCGTGTTTGACGAATGCGGAATCACAGACGATCAGCTCCTGGCTCTGCTCCCTGTCCCTGGGAGACCCTAAGAAACTGCT CACCCAACACTTTGTGCAAGAGAATTACCTCGAGTATAGGCAAGTGCCTGGCTCCGACCCTGTGAGGCTCTGGAAGCCCAACAGGAAGCCCTCG GCCTCGTGTGTGTGCAAGCCGCTACCTCCAGCTCCAGCCCTTGGTCCTGGGAACCCTCGAGTTTTACCTCGCCATGCCCTTTGCCACACCCATGGAG GCTGAGCTCGCCAGAAGGTCCCTGGCTCAGGATGCCCCTCCCCCTCCCCGTCGAGGAAGCCCCTAGGGGAGTGAGAATGGCTGCCAGACTGCAAGGCGC TGCCTGGAGACTGGAACCCGAAGACGGAACCGCTCTGTGTTTCATTTTCGCTGCCGAGCAATTCTCCGACGAAGTGGAACCCGCTACCCCTGAGGAAG GCGAACCCGCTACCCAAAGGCAAGACCCTGCCGCTGCCCAAGAGGGAACCATGAACTATCCCCTCTGGTCCCAGTCCTACGAAGACTCCAGCAATCAG TCTGTCCAGGAAAGTGGCTGGGCTCGTGCATGTGGATCTGTTTCTGAAAGAGGGGAGCCTGTGACGAACTGTTTAGCTATCTGATTGAGAAAAGTGAAAA CTCATGTGGATCACAGCCGCTATGCCTCTGGAACAGAGAAGCCAACACTGTAAGCCTGAGGAAGGCCTCGAGGCTAGGGGAGAGGCTCTGGGACTGGT ACGARTTCCTCTGGGGACCCAGAGCCCTCGTGGAAACCTCCTACGTCAAGGTCCTGCATCACATGGTGAAAATCTCCGGCGGACCCCATATCACAAAC TGTAGGCTCAGCGAAGGCGATGTGATGCACCTCAGCCAAAGCCCTTAGCGTCAGCCTAACTGTCCGTGCTCAGCCTCAGCGGAAACTATCTGGAATACAG ACAGGTCCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCTAGGGCTCTGGTCGAGACAAGCTATGTGATTTTCTCCAAGGCTAGCTCCA AGAGGCAGACTGGATCAGCTCCTGAGACACGTCATGAATCCCCTCGAGACACTGTCCTACATTGCCCAATTCACAAGCCAATTCCTCAGCCTCCAGTG TCTGCAAGCCCTCTACGTCGACTCCCTGTTTTTCCTCAGGGGAAGGCTCGGCCAACACCTCCACCTCGAGACATTCAAAGCCGTCCTGGATGGCCTCG CTCCAGCAACTGTCCCTGCTCATGTGGATCACATGCTGTAAGAAACTGAAAATCTTTGCCATGCCCATGCAGGATATCAAAATGATTCTGAAAATGGT

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CCAGCTCGACTCCATCGAAGACCTCGGCGCTCCCAGAGGCCCTCACGGAGGCGCTGCCTCCGGCCTCAACGGATGCTGTAGGTGTGGCGCTAGGGGAC CCGAAAGCAGACTGCTCAAGAAAGTGGCTGACCTCGTGGGATTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGAG TAGCATTAGCGCTCTGCAAGCCTCATCGGACACCTCATCGGACTGCCAACCCTCACCCATGTGCTCTACCCTGTGCCTCTGGAAAGCTATATCGCTA GGGAAGGCGATTGCGCTCCCGAAGAGAAAATCTGGGAGGAACTGTCCGTGCTCGAGGTCTTCGAAGGCAGAGAGGATAGCATTGACCAACTGCTCAGG CATGTGATGAACCCTCTGGAAACCCTCAGCATTACCAATTGCAGACTGTCCGAGGGGAGACGTCATGCATCTGTCCAGGGCTCTGGCTGAGACAAGCTA ATGGCCCAAGGCGCTATGCTCGCCGCTCAGGAAAGGAGGTGCCTAGGGCTAAGAATTACAAACACTGTTTCCCTGAGATTTTCGGAAAGGCTAGGGA AAGCCTCCAGCTCGTGTTTTGGCATTGACGTCAAGGAAGCCGATACCCTCGTGGAAGTGACACTGGGAGAGGGTCCCCGCTGCCGAAAGCCCTGACCCTC AATCCCTGTCCCCATTGCGGAGACAGAGTGATGCTGACAGACGTCAGCCCTGAGCCTTCTGCAAGCCCTCCTGGAAAGGGCTAGCGCTACCCTCCAGGA TCTGGTCTTCGATGAGTGTGAGGATGAGGGAGCCTCCGCCGGACAGGGACCCAAACCCGAAGCCGATGCCAAGAGCAAGGCCATCCCCAAACCCGAT GGAGCCGCTATGTCCTGGAGAGGCAGAAGCACATACAGACCCAGAAGGTATGTGGAACCCCTGAGATGATGGACCCATGAGGCCTTACAT TAGCATGAGCGTCTGGACAAGCCCTAGGAGACTGGTCGAGCTCGCCGGACAGTCCCTGCTCAAGGATGAGGCTCTGGCTATCGCTTACGATGGCAGAG AGCATAGCGCTTACGGAGAGCCTAGGAAACTGCTCACCCAAGACCTCGTGCAAGAGAAATACCTCGAGTATAGGCAACAGTGTTTCCTCCCCGTCTTC GCATGAGTGGGTGCTCAGGGAAGGGGGAACAGCTCCACATTACCATGCCCCTTTAGCTCCCCCATGGAGGGCTGAGGTCGTGAGAAGGATTCTGTCCAGG ATGCCGCTCCCCTCGCGAGTGCTCCTGAAAGAGTTTTACCGTCAGGGGAAACATTCTGACAATCAGACTGACAGCCGCTGACCATAGGCAA CTGCAACTGTCCAAGATGATCCTCAAGATGGTGCAACTGGATAGCATTGAGGATCTGGAAGTGACATGCACATGGAAACTGCCTACCCTCGCCAAATT CTCCTTCCTCATCATTGTGCTCGTGATGATCGCTATGGAAGGCGGACACGCTCCCGAAGAGGAAATCTGGGAGGAACTGTCCGTGATGGAGGTCGAGG TCACCTGTACCTGGAAGCTCCCCACACTGGCTAAGTTTAGCCCTTACCTCGGCCAAATGATTAACCTCAGGAGACTGCTCCTGTCCGAGGGACTGGAA ${\tt CGAATGGGTCCTGAGAGAGGGAGGGAGGGAGCCGCTCACATTCACGCTCAGCTCCTGAGATAGCCCTGAGAAAGAGGGAACAGTATATCGCTCAGTTTACCT}$ CCCAGTTTCTGTCCCTGCAATGCCTCGGCAATGCCGGAGGCCCTGGCGGAGGCCGCAGGCGGAAGGCGGAAGGCGAAGGCGCAGAGGCGCTGCCGGA GCCTCCGGCCCTGGCGGAGGCCCTAGGGGAGCCGGAGCCGTAGGGGTAGCGGACCCGGAGGCGCGGAGCCCCTAGGGGGACCCCATGGCGGAGCCGCTAG CTCTGGCTAGGAGAAGCCTCGCCCAAGACGCTCCCCCTCTGCCTGTGCCTGGCGTCCTCAAGGAATTCACAGTGTCCGGCAATATCCTCGCCGCT TTCGATGGCAGACACTCCCAGACACTGAAAGCCATGGTGCAAGCCTGGCCCTTTACCTGTCTGCGTGTGCTCATGAAAATCAAAGTGTCCGC CAGAGTGAGATTCTTTTTCCCTAGCCTCAGGGAAGCCGCTCTGAGAGAGGGAAGGGGAAGGCGTCGCCGCTGGCATTACCGATGACCAACTGCTCGCCC TCCTGCCTAGCCTCAGCCATTGCTCCCAGCTCACCACTGTCCTTCTATGGCAATAGCATTGTGAAAACCCCTGAGGAAGAGATGAGGTCCCACTAT GTGGCTCAGACAGGCATTCTGTGGCTGCTCATGAATAACTGTTTCCTCAACCTCATCTCCAGCTGTCTGCAACAGCTCAGCCTCCTGATGTGGATTAC aaaagctcaagattttcgctatgcctatgccaagacattgccagagagcctgtgacaaaggctgagatgctggaaagcgtcatcaaaaacttataagcat TGCTTTCCCGAAATCTTTGGCAAAGCCTCCCTGGTCAGGAGAATCCTCAGCAGAGACGCTGCCCCTCTGCCCTAGGCCTGGCGCTGTGCTCAAGGATTT CACAGTGTCCGGCAATCTGCTCCACTGTAGCCAACTGACAACCCTCAGCTTTTACGGAAACTCCATCTCCATCTCCAGCCCTCCAGTCCCTGCTCCAGC ATCTGATTGGCCTCATGGCTCAGCGCTAACCCTTGCCCTCACTGTGGCGATAGGACATTCTATGACCCTGAGCCTATCCTCTGCCCTTGCTTT ATGCCTGCCGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGAGAGACTGCCTAGCCAACCCATTATCCATACCTGTCT GCTCCAGGCTAGGCTCATGAAAGAGGAAAGCCCTGTGGTCAGCTGGAGGCTCGAGGCTGAGGATGGCACAGCCCTCTGCTTTATCTTTTGTGTATTTCT TTCTGCCTGACCATCTGGGAAGGCCTTTCCATCTGAATTTCTGTGACTTTCTGGCTGCCCCCTATCTGGGACAGATGATCAATCTGAGAAGG CTCCTGCTCAGCCATATCCATGCCTCCAGCTATATCTCCCCCGAAAAGGAAGAAGCAACAGGCTCCCGCTACCGAAGAGCAAGAGCTGCCTCCAGCTC AGCATCTGCATCTGGAAACCTTTAAGGCTGTGCTCGACGGACTGTCCACCGAAGCCGAACAGCCTTTCATTCCCGTCGAGGTCCTGGTCGACCTCTTC CTCAAGGAAGGCGCTTGCGATGAGCTCTTCTCCGCCGAAGTGCCTGGCGGTCAGGGAAGGCCAAGGCCCTAGGGGAAGGGAAGAGCTCCCAGAGGCGT CCGATAGCAGACTGCTCGGCCCTAGGGGAGCCGGAGCCGCTAGGGGCTAGCGGACCCAGAGGCCGCAGGGCCCCTAGGGGGACCCCATGGCGGAGCCGCTAGC GGAGCCTGCCACACAGAGACAGGATCCCGCTGCCGCTCAGGAAGGCGAAGACGAAGGCGCTAGCGCTGAGGCCCTAAGCCTGAGGCTCCCGAAG CCGCTCAGCCTATGACAAAGAAAAGGAAAGTGGATGGCCTCAGCACAGAGGCTGAGCAACCCTTTATCCCTGTGGAAGTGCTCGGCAGATGCCCTTGC GGAGCCAGAAGGCCTGACTCCAGGCTCCTGCAACTGCATATCACAATGCCTTTCTCCAGCCCTATGGAAGCCGAACCCGGAGCCGTCCTGAAAGACTT TACCGTCAGCGGAAACCTCCTGTTTATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCCGAGGATATCCATGGCACACTGCATCTGGAAA GGCTCGCCTATCTGCATGCCAGACTGAGAGAGCTCCTGTGTGAGCTCGGCAGACCCTCCGACTCCCAGGAACAGGGACACCCTCAGACAGGCTGTGAG TGTGAGGATGGCCCTGACGGACAGGAAATGGATCCCCCTAACCCTGAGGAATTCGTCATCGGACTGAGAGTGTGGCAGTGGGAGGTCATCTCCTGCAA ACTGATTAAGAGAGCCACAACCAGCAGACAGCCTGCCGCTGACGCACGGACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGAC CCGGAGAGGCTGCCGCAGAGGCCACAGGCCATAGCTATGTGCTCGTGACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAAC ATACTTTTTCCCTACCGGAATCCTCTGGCTCCTGATGAACAATTGCTTTCTGAATCTGTCCCCAGAAAGCCTGCCGCTGAGTTTCAGGCTGCCCTCA GCAGAAAGGTCGCCGAACTGGTCCACTTTCTGCTCCTGAAATACAGAGGCCAGAGAGCCTGTGACAAAAGGCTGTGCCTGACTACCTGCCAGACACCTGCCAGATAC GAATTCCTCTGGGGACCCAGAGCCCTCGCCGAAACCTCCTACGTCAAGGTCCTGGAATACGTCGGCTGTTTGCAGATGCGGAGCCAGAGGCCCTGAGTC CAGGCTCTGGAATTCTATCTGGCTATGCCTTTCGCTACCCCTATGGAAGCCGAAGCCACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCCGATA ACCARATCATGCCCARAGCCGGACTGCTCATCATTGTGCTCGCCATTGGCAATGCCGGAGGCCCTGGCGGAGCCGGAGCCACAGGCGGAAGGGGGACCC AGAGGCGCTGCCAGAGCCTCCGGCCCTAGGGGA

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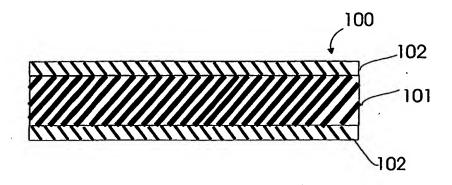


FIGURE 28

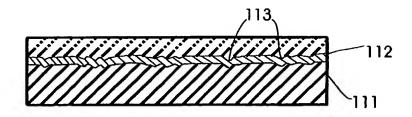


FIGURE 29

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Cassettes for construction of a full-length HIV Savine

Cassette Al

ggatccaccATGACAGGCCCTTGCACAAACGTCAGCACCGTGCAATGCACACACGGAATCAGACCCGTCGTGTCCA CCCAACTGCTCCTGAATGGCTCCCTGAGAAGCCTCTACAATACCGTCGCCACACTGTGGTGCGTCCACCAAAGGAT TGACGTCAGGGACACAAAGGAAGCCCTCGACAAAATCGAACTCGGCGATGGCGGAGGCGCTGAAAGGCAAGGCACC TCCAGCTCCTTCAACTTTCCACAAATCACACTGTGGCAAAGGCCTCTGGTCACCGAACCCTTCAGAAAAAAGAATC CCGATATGGTGATTTACCAGTACATGGACGATCTGTATGTGGGAAGCGATCTGGAAATCGGACAGCATTTTACCAC ACCCGATAAGAAACACCAAAAGGAACCACCATTCCTCTGGATGGGATACGAACTGCATCCCGATAGGTGGACCGTC CAGCCTCTTAATTTCCCTCAGATTACCCTCTGGCAGCGTCCCCTCGTGACAATCAAAATCGGCGGACAGCTCATAG AGGCTCTGCTCGACACAGGCTCCTATGGCAGAAAGAAACGTAGGCAACGTAGACGCGCTCCTCAGAGCAGCAAGGA TCACCAATACCCTATCTCTGAGCAACCCCTCTCCTTCTTTAGGGAAAACCTGGCTTTCCAGCAAGGTAAAGCCAGA GAGTTTTCCAGCGAACAGACAAGAGCCCAATAGCTCCGCCTCCAGGAAGAGCCCCCAAATCTCCGGCGAAAGCTCCG TCATTCTGGGATCTGGCACCAAAAACGCCGCTACTAGAAGAATCGAAGTGAAAGATACCAAAGAGGCTTTGGATAA GATTGAGGAGGTGCAAAAGAAAAGCGAGCAAAAGACACAACAGGCTGCCGCTAAAGCCGGATACGTCACCGATAGG GGAAGGCAAAAGATTATCTCCCTGACAGAGACAACCAATCAGAAAACCGAACTGCATGCCATTCAAGAAGCCACTA CCACACTGTTTTGCGCCAGCGATGCCAAAGCCTATGAGACAGAGGTCCACAATGTGTGGGCCACACACGCTTGCGT CCCCGCTGACGATACAGTGCTGGAGGAGATGAACCTCCCCGGAAAATGGAAGCCTAAGATGATTGGCGGAATCGGC GGATTCATTAAGGTGAGAAAAATCGGACCCGAAAACCCTTACAATACCCCAATCTTCGCTATCAAGAAAAAGGACT CCACCAAATGGAGAAAGCTCGTGGATTTCAGAGTTAGGATTATCAATATCCTCTACCAAAGCAATCCCTATCCTAG CTCCGAAGGCTCCAGGCAAACCAGAAAGAATAGGAGAAGGAGATGGGGAGGCGAACGGGGTAGGGATAGGTCCGTG AGACTGGTCAACGGATTCTTAGCCCTCGCCTGGGACGATCTGAGAAACCTCTGCCTCTTCGAAAACCTCTGGGTCA CCGTCTACTATGGCGTCCCCGTCTGGAGAGAGGCTGCCACAACCCTCTTCTGTGCCTCCGACGCTAAGGCTTACGC TGCCATGGCTGGCAGAAGCGGCGCACAGACGAAGAGCTCCTGAGGGCTATCAGAATCATTAACATTCTGTATCAG TCCAACCCTTACCCTTCCGCTAGTATGAGAATCAGAACCTGGAACAGCCTGGTCAAGCATCACATGCACATCTCCA AGAAAGCCAAAGGCTGGTTCTATAGGCATCACTTTGAGGAGCTCGAGCTCGTGAATCAGATTATCGAAAAGCTCAT CAAAAAGGAAAAGGTCTACCTATCATGGGTACCAGCCCACAAGGGAATCGGACAAACCAAAGAGCTCCAGAAACAG ATTATCAAAATCCAAAACTTTAGGGTCTACTATAGGGATAGCAGAGACCCTATCTGGAAGGGACCCAAAAGCTTTG TCTGAAACCCGAACCCACAGCCCCTCCCGCTGAGAATTTCAGATTCGGTGAGGAAACTACACCCTCCCAAAAGCAA: GAGCAAAAGGATAAGGAGCAATACGATCAGATTCTTATTGAGATTTGCGGCAAGAAAGCTATTGGTACGGTGCTCG TGGGACCTACCCCTGTGAATATCATTGGCAGAATTTACGAAACCTATGGCGATACCTGGGAGGGCGTCGAGGCTCT GATCAGAATCCTCCAGCAACTGATGTTTATCCATTTCAGAATCGGATGTTTTCATTGCCAAGTGTGTTTTCTCACC AAAGGTCTCGGCATTAGCCACGGAAGGAAAAAGAGAAAACAGAGAGGGGAGCTCCCCAAGCTGCCATGGACCCCG TGGACCCCAAGCTGGAGCCTTGGAAACACCCTGGCTCCCAGCCTAAGACAGCCTGTTACAAATGCTATTGCAAAAA CTCAAGTCCCTGTTTGGCAATGACAATTTCAATATGTGGAAGAATGACATGGTGGAACAGATGCAAGAAGACATTA TCTTACTATGGGACCAAGCCTCAAGCCTTGCGTCAAGCTCGACGTCGGCGATGCCTATTTCTCCGTGCCTCTGGA GGCCAAGTGAATTGCTCACCAGGCATTTGGCAACTGGATTGCACACACCTGGAGGGAAAGATTATCCCTAAGGTCA TAGCATGGATGACCTCTACGTCGGCTCCGACCTGG

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AGATTGGCCAACATAGGACCAAAATCGAAGAGCTCAGGGAACACCTCCTGAAATGGGGACTCACCGAAACCACAAA CAGACAATGGCAGGACAAAGATTGAGGAACTGAGACCGCATCTGCTCAAATGGGGCTTCACAACCCCTGACAAAAA AAGAGACGCAGAGAAAATCACACAATGAATGGCCATACTGCCACAGAGTCCCAGAATCAGCAAGACAGAAACGAAA AGGAACTGCTGGAGCTCGACAAATGGGCAAGCCTCTGGAATTGGTTTAACATTACCGACACCGGAAATAGCTCCAA AGTGTCCCAGAATTACCCTATCGTCCAGAATGTCCAAGGCCAAATGGTCCACCACCCCTCTCCCCCAGACTCATC GGACTGAGAATCGTTTTCGCTGTGCTCAGCATTATCAATAGGGTCAGGCAAGGCTATAGCCCTCTGTCCTTCCAAA CCCTCCCCTCATCCATCTGCAATACTTTGACTGTTTCGCTGACTCCACCATTAGGAGAGCCATCTTGGGACACAT AGTGAGAAGGAGATGCGAATACGCTGTGGGACTCGGAGCCATGTTCCTTGGCTTTCTGGGTGCCGCTGGCTCCACC ATGGGCGCTGCCTCCATGACACTGACAGTGCAAGCCTATGACCCTAGCAAAGACCTCATTGCTGAGATTCAGAAAC AGGGCCAGGGTCAGTGGACATTTCAGATTTTCCAAGAGCCTTTCAAAAACGGAACCGTCCTGGTCGGCCCTACACC CGTCAACATCATCGGAAGGAACATGCTGACACAGCTTGGCCGCACTCTCAACTTTCCCATTAGCAAAGGCAGCCCT GCTATCTTTCAGTCCAGCATGCCACAGATTCTGGAGCCTTTTAGGATAAAAAACCCTGAGATGGTCATCTATCAGT ATCCTAGCCCTCTGACATTCGGATGGTGTTTCAAACTGGTCCCCGTGGACCCCAGCGAAGTGGAAGAGATCAACAA GGGCGAAAACAATTGCCCCCTGTTTAGGAAATACACAGCCTTTACCATTCCCTCCATCAATAACGAAACCCCTGGC ATTAGGTATCAGTATAACGTCCTCAGGGATGGGGAAGCACAATGGGAGCCGCCAGCATGACCCTCACCGTCC AGGCTAGGCTACTGCTCAGCGGAATCGTCCAGCAACAGAGCAATCTGCTGGAGGAGAATAGGGAAATCCTCAGAGA GCCTGTGCATGGCGTCTACTACGATCCCTCCAAGGATCTGGTCGCTGAAATCCAAAAGCAAGGCAGAGGAACTG TCCACCATGGTGGATATGGGAAACTACGACCTCGGAGTGGACAATAACCTCGCCGCTATTAGAATCCTGCAACAGC TCATGTTCATTCACTTTAGGATTGGCTGCCAGCACTCCAGGATTGGCATCATCCGTCAGAGAGGAGGGCCAGAGCTCC ${\tt CAGGAAAAAGGGATGCTGGAAGTGTGGCAGAGAGGGGACACCAGATGAAGGATTGCACTGAGAGACAGGCTAACTTT}$ ATGGCGTCAGCATTGAGTGGAGGATAAGGGAAAGGGCTGAGGATAGCGGCAACGAAAGCGAAGGCGACACAGAAGA GCTCAGCACATTGGTGGACATGGGCAATTACGATCTGTCTAGCCCTGCCCCCAGGGGACCCGATAGGCTGGAGAGA ATCGAAGAGGAAGCCGGAGAGCAAGGCAGAGCCTCAGGCTCGTGAATGGCAGAGAGGTCGAGGAAGTCA GTGGCCAGCTTCTCTCCGAGCAAACAGGGGCTAACTCCTCTACAAGCAGAAAGCTGGGAGACGGAGGCGGAGCCG ACAGACAGGGAACAAGCTCCAGCTGTTTCAATTGCGGCAAAGAGGGGACACATTGCCAAAAACTGTAGGGCCCCTCG CAAGAAAGGTTGTTGGAAATGCGGAAAGGAAGGCCATCAAATGAAAGACTGTACCGAAAGGCAAGCCAATTTCCTC GGCAAAATCTGGCCCTCCAACAAAGGCAGACCCGGAAACTTTCTCCAAAGCAAATGGCTCTGGTATATCAAAAATCT TTATCATGATCGTCGGTGGACTGATTGGCCTCAGGATTATCTTTGCCGTCCTGTCCATCGTTAACGGAGCCGTGAG CCGAGACCTCGATAAACATGGCGCTATTACAAGCTCCAATACCGCTGCCAATAACGCTGACTGTGTCTGGCTGAAG GCTGCTGCCATGACACCCCTGGAGATCATCGCTATCGTCGCCTTTATCGTCGCCCTCATCATAGCCATTGTGGTCT GGACAATCGTCTACATTGAGTATGTCGACtgaagatctgaattc

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A2 fragment

ggatccaccATGACAGGCCCTTGCACAAACGTCAGCTCCGTGCAATGCACACAGGAATCAAACCCGTCGTGTCCA CCCAACTGCTCCTGAATGGCTCCCTGAAAAGCCTCTACAATACCGTCGCCACACTGTGGTGTCCCACCAAAGGAT TGAGGTCAAGGACACAAAGGAAGCCCTCGACAAAATCGAACTCGGCGATGGCGGAGGCGCTGAAAGGCAAGGCACC TCCAGCTCCATCAACTTTCCACAAATCACACTGTGGCAAAGGCCTCTGGTCACCGAACCCTTCAGAAAAGAGAATC CCGAAATGGTGATTTACCAGTACATGGACGATCTGTATGTGGGAAGCGATCTGGAAATCGGACAGCATTTTACCAC ACCCGATAGGAAACACCAAAAGGAACCACCATTCCTCTGGATGGGATACGAACTGCATCCCGATAGGTGGACCGTC CAGCCTTTTAATTTCCCTCAGATTACCCTCTGGCAGCGTCCCCTCGTGACAATCAAAATCGGCGGACAGCTCATAG AGGCTCTGCTCGACACAGGCTCCTATGGCAGAAAGAAACGTAGGCAACGTAGACGCGCTCCTCAGAGCAGAAAGGA TCACCAATACCCTATCTCTGAGCAACCCCTCTCCTTCTTTAGGGAAAACCTGGCTTTCCAGCAAGGTAAAGCCAGA GAGTTTTCCAGCGAACAGACAGGAGCCAATAGCTCCGCCTCCAGGAAGAGCCCCCAAATCTCCGGCGAAAGCTCCG TCATTCTGGGATCTGGCACCAAAAACGCCGCTACTAGAAGAATCGATGTGAGAGATACCAAAGAGGCTCTGGATAA GATTGAGGAGGAGCAAAACAAAAGCAAGCAAAAGACACAACAGGCTGCCGCTAAAGCCGGATACGTCACCGATAGG GGAAGGCAAAAGATTATCTCCCTGACAGAGACAACCAATCAGAAAACCGAACTGCCATTCAAGAAGCCGATA CCACACTGTTTTGCGCCAGCGATGCCAAAGCCTATGACACAGAGGTCCACAATGTGTGGGCCACACACGCTTGCGT CCCCGCTGACGATACAGTGCTGGAGGAGATGAACCTCCCCGGAAAATGGAAGCCTAAGATGATTGGCGGAATCGGC GGATTCATTAAGGTGAGAAAGATCGGACCCGAAAACCCTTACAATACCCCAATCTTCGCTATCAAGAAAAAGAACT CCACCAAATGGAGAAAGCTCGTGGATTTCAGAATTAGGATTATCAAAATCCTCTACCAAAGCAATCCCTATCCTAG CTCCGAAGGCACCAGGCAAACCAGAAAGAATAGGAGAAGGGGGATGGGGAGGCGAACAGGGTAGGGATAGGTCCGTG AGACTGGTCAACGGATTCTTAGCCCTCGCCTGGGACGATCTGAGAAGCCTCTGCCTCTTCGACAACCTCTGGGTCA CCGTCTACTATGGCGTCCCCGTCTGGAGAGGGCTAACACACCCTCTTCTGTGCCTCCGACGCTAAGGCTTACGC TGCCATGGCTGGCAGCAGCAGCAGACGAAGAGCTCCTGAAGGCTGTCAGAATCATTAAGATTCTGTATCAG TCCAACCCTTACCCTTCCGCTAGTATGAAAATCAGAACCTGGAAGAGCCTGGTCAAGCATCACATGTACATCTCCA AGAAAGCCAATGGCTGGTTCTATAGGCATCACTTTGAGGAGTCCGAGGTCGTGAATCAGATTATCGAAAAGCTTAT CAAAAAGGAAAAGGTCTACCTATCATGGGTACCAGCCCACAAGGGGAATCGGACGAACCAAAGAGCTCCAGAAACAG ATTATCAAAATCCAAAACTTTAGGGTCTACTATAGGGATAGCAGAGACCCTATCTGGAAGGGACCCAAAAGCCTTG TCTGAGACCCGAACCCACAGCCCCTCCCGCTGAGAATTTCGGATTCGGTGAGGAAACTACACCCTCCCAAAAGCAA GAGCCAAAGGATAAGGAGCAATACGATCAGATTATTATTGAGATTTGCGGCAAGAAAGCTATTGGTACAGTGCTCG TGGGACCTACCCCTGTGAATATCATTGGCAGAATTTACGAAACCTATGGCGATACCTGGGAGGGGTCGAGGCTCT GATCAGAATCCTCCAGCAACTGATGTTTATCCATTTCAGAATCGGATGTTTTCATTGCCAAGTGTGTTTTCTCACC TGGACCCCAACCTGGAGCCTTGGAAACACCCTGGCTCCCAGCCTAAGACAGCCTGTAACAAATGCTATTGCAAAAA GTGCCCTAGCGAAGAGACACCCCTAGCCAGAAACAGGAACAGAAGAACAAAGAACTCTACCCCCCTTTAGCCAGC CTCAAGTCCCTGTTTGGCAATGACAATTTCAATATGTGGAAGAATAACATGGTGGAACAGATGCAAGAAGACATTA TCTCACTATGGGACCAAAGCCTCAAGCCTTGCGTCAAGCTCGACGTCGGCGATGCCTATTTCTCCGTGCCTCTGGA GGCCAAGTGAATTGCTCACCAGGCATTTGGCAACTGGATTGCACACCCTGGAGGGAAAGATTATCCCTAAGGTCA TAGCATGGATGACCTCTACGTCGGCTCCGACCTGGAGATTGGCCAACATAGGACCAAAATCGAAGAGCTCAGGGCA

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EACCTCCTGAGATGGGGACTCACCGACACCACAAACCAAAAGACTGAGCTCCACGCTATCCATCTGGCTCTGCAAG ACTCCGGCTTAGAGGTCAACATTGTGACAGACATTCCCGCTGAGACTGGTCAAGAGACCACCTATTTCATTCTGAA ACTGGCTGGCAGATGGCCTGTGAGAATCATTCACACAGACAATGGCAGGACAAAGATTGAGGAACTGAGACCGCAT CTGCTCAAATGGGGCTTCACAACCCCTGACAAAAAGCGTCAGAAAGAGCCTCCCTTTCTGTCTAGTGTCAAGAAAC CACAGAGTCCCAGAATCAGCAAGACAGAAACGAAAAGGAACTGCTGGAGCTCGACAAATGGGCAAGCCTCTGGAAT TGGTTTAACATTACCGACACCGGAAGTAGCTCCCAAGTGTCCCAGAATTACCCTATCGTCCAGAATCTCCAAGGCC AAATGGTCCACCAACCCATCTCCCCCAGACTCGTCGGACTGAGAATCATTTTCGCTGTGCTCAGCATTATCAATAG GACTCCACCATTAGGAGAGCCATCCTTGGACACAGAGTGAGCAGGAGATGCGAATACGCTGTGGGAATCGGAGCCA TGTTCCTTGGCTTTCTGGGTGCCGCTGGCTCCACCATGGGCGCTGCCTCCATCACACTGACAGTGCAAGCCTATGA CCCTAGCAAAGACCTCATTGCTGAGATTCAGAAACAGGGTCAGGATCAGTGGACATATCAGATTTTCCAAGAGCCT GCACCCTCAACTTTCCCATTAGCAAAGGCAGCCCTGCTATCTTTCAGTCCAGCATGACACAGATTCTGGAGCCTTT TAGGAAACAAAACCCTGACATGGTCATCTATCAGTATCCTAGCCCTCTGACATTCGGATGGTGTTTCAAACTGGTC CCCGTGGACCCCAGCGAAGTGGAAGAGACCAACAAGGGCGAAAACAATTGCCTCCTGTTTAGGAAATACACAGCCT TTACCATTCCCTCCACCAATAACGAAACCCCTGGCATTAGGTATCAGTATAACGTCCTGCCTCAGGGATGGGGAAG CACAATGGGAGCCGCCAGCATGACCCTCACCGTCCAGGCTAGGCAACTGCTCCAGCGGAATCGTCCAGCAACAGAAC **AATCTGCTGGAGGAGAATAGGGAAATCCTCAAAGAGCCTGTGCATGGCGTCTACTACGATCCCTCCAAGGATCTGA** TCGCTGAAATCCAAAAGCAAGGCACAGAGGAACTGTCCGCCTTGGTGGATATGGGAAACTACCACCTCGGAGTGGA ATTGGCATCATCCGTCAGAGAAGGGCCCAGAGCTCCCAGGAAAAAGGGATGCTGGAAGTGTGGCAAAGAGGGACACC AGATGAAGGATTGCACTGAGAGACAGGCTAACTTTCTGGGAAAGGATGCCAGACTGGTTATCAAAACCTATTGCGG ACTGCATACCGGTGAGAGAGACTGGCACCTCGGCCATGGCGTCAGCATTGAGTGGAGGACAAGGGAAAGGGCTGAG GATAGCGGCAACGAAAGCGAAGGCGACAGAGAAGAGCTCAGCACAATGGTGGACATGGGCAATTACGATCTGTCTA GCCCTGCCCCAGGGGACCCGATAGGCTGGAGAGAATCGAAGAGGAGGAGGCGAGAGACAGAGACAGAAGCCGT CAGGCTCGTGAATGGCAGTGAGGGCGAGGAAGTCAATAAGGGAGAAATAACTGTCTGCTCCACCCTATGAGTCAA GGGATTACGGAAAGCAAATGGCTGACGATGACTGTGTGGCCGGCTTCTCTTCCGAGCAAACAAGGGCTAACTCCCC TGCAAGCAGAAAGCTGGGAGACGGAGCCGACAGACAGGCAACAAGCTCCAGCTGTTTCAATTGCGGCAAA GAGGGACACATTGCCAAAAGCTGTAGGGCCCCTCGCAAGAAAGGTTGTTGGAAATGCGGAAGGGAAGGCCATCAAA TGAAAGACTGTACCGAAAGGCAAGCCAATTTCCTCGGCAAAAATCTGGCCCTCCAAAAAAAGGCAGACCCGGAAACTT TCTCCAAAGCAAATGGCTCTGGTATATCAAAATCTTTATCATGATCGTCGGTGGACTGATTGGCCTCAGGATTATC TTTGCCGTCCTGTCCATCATTAACGGGGCCGTGAGCCCGAGACCTCGATAAACATGGCGCTATTACAAGCTCCAATA $\tt CCGCTGCCAATAACCCTGACTGTGTCTGGCTGGAGGGCTGCTGCCATGACACCCCTGGAGATCATCGCTATCGTCGC$ CCTTATCGTCGCCCTCATCATAGCCATTGTGGTCTGGACAATCGTCTACATTGAGTATGTCGACtgaagatctgaa ttc

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B1 fragment

qqatccaccATGCTCGAGAATATGCTCACCCAAATCGGATGCACACTGAATTTCCCTATCTCCCCCATTGAGACAG TGCCTGTGAAACTGAAACCCGGAATGGATGGCGCCGCCACCTTTAGGCCTGGCGGAGGCAATATCAAAGACAATTG GAGAAGCGAACTGTATAAGTATAAGGTCGTGAAGATTAAGCCTCTGGGAATCACATGGATTCCCGAATGGGAGTTC GTCAACACCCCCACTGGTCAAGCTATGGTATCAGCTGGAGAAAGACCCTATCGTTGGCGTTGAGCCTCAGGATC CTCTGTCCTGTTTCTGGATGGCATTGACAAGCTCAAGAGGAACATGAAAAGTATCACTCCAACTGGAGGACAATG GCCAACGACTTTAATCTGATGAAGCATCTCGTCTGGGCCTCTAGGGAGCTGGAGAGATTCGCTCTGAATCCCAGCC TGTCAAAACCATTATCGTCCAACTCAACGAAAGCGTCGAGATTAACATGGGCGCTAGGGCTAGTGTCCTCAGAGGC GCCTGGAGGGACTGGTTTACTCCAAAAAGAGGCAAGACATTCTGGATCTGTGGGTGTATAACACACAGGGATTCAC TAGATGGGGAACCATGATCCTCGGCTTGGTGATTATCTGTAGCGCCAGCGAGAATCTGTGGGTGACAGTGTATTAC GGAGTGCCTGTGGGGGGGGGCACCTCCTGTCCGGCATTGTGCAACAACAAAATAACCTCCTGAGGGCTATCGAAG $\tt CCCAACAGCATCTGCTCCAGCTCACCGTCTGGGTCAGGCATTTCCCCAGGCCTTGGCTCCACGGCCTGGGACAGTA$ CATCTATGAGACATACGGAGACACATGGGCGGGAGTGGAAGCCCTCACAGCCCTCATCACACCCCAAAAAGATTAGG CCTCCCTCCCATCCGTGAAAAAGCTCACCGAAGACAGATGGAATGAGCCTCAAAAGACATATAGCGCTGGCGAAA GGATTATCGATATCATTGCATCCGACATTCAGACTAAGGAACTGCAAAAGCAAATCCTAAAGATTCAGAATTTCGC TGTGTTTATCCATAACTTTAAGAGGAAGGGAGGCATTGGCGGCTACTCCGCCGGAGAGAATCATTGACATTATC GCCACCGATATCATTCCCGTGGGCGAAATCTATAAGAGATGGATCATTCTGGGACTCAACAAAATCGTGAGAATGT ATCTACCCGTCAGCATTCTGGATATCAGAGTGAGACAGGGATACTCCCCCCTCAGCTTTCAGACACTGCTGCCCGC CCTCTGCCTCAGACAAGGGGAGACAATCCCACAGACCCTAAGGAAAAGGCAAAAAAGGCTAGTGGAGGGGTCGAGTCCA TGAATAAGGAACTGAAAAAGATTATCGGACAGGTCAGGGACCAGGCTGAGCACCTGAAAACCGCTGTGCAAATGGC TGCCATGCAGATGCTCAAGGATACCATTAACGAAGAGGCTGCCGAGTGGGACAGAGTCCATCCCGTCCATGCCGGG CCCGTTCCCCCTCTCACCGAGATTTGTAAAGAAATGGAAAAAGAAGGCAAAATCTCCAAGATTGGCCCTGAGAATC CCTATAACACACCCATCTTGCCATTCAAGTGAGAGAGGCAAGCCGAACACCCTCAAGACAGCCGTCCAGATGGCAGT GACTTTAGGGAGCTCAACAAACGTACACAGGATTTCTGGGAGGTCCAGCTCGGCTTTTTGGCTCTGGGTTGGGATG ACCTCAGGAGCCTGTGTCTGTTCAGCTATCACAGACTGAGAGACTTTATCCTCATCGTTGCCAGAATCTGCCGACA TAGCAGAATCGGCATCACTAGGCAACGTAGAGGTAGGAACGCGCCCCCAGTTCCGCTGCCCCCAAAATCTCCTTC GACCCCATTCCCATTCACTATTGCGCTCCCGCTGGCTTCGCTATCCTCAAGTGTAACGATAAGAACTTCAATGGCG AAGAGGATTGGCATCTGGGACAGGGAGTGTCCATCGAATGGAGACAGAAAAGCTATAGCACACAGGTGGACCCTGA CCTCGCCGATCAGCCTAGCCTCTATCCTCCCTTAGCTTCCCTGAAAAGCCTCTTCGGAAACGATCCCTTATCCCAA GCCGCTAGAAGGGCTATCCTCGGCCATATAGTCAGGAGAAGGTGTGAGTATCAGTCCGGACACAATAAGGTCGGCT CCCTGCAATACCTCGCACTCAGTCAACCCACAACCGCTTGCTACAAGTGTTACTGTAAGAAATGTTGCTTCCACTG AGCAGGCAAGACGAAGACGCAAGCCAAGTACCATAGCAATTGGAGAACCATTGGCAATGAGTTTAACCTCCCCCCTA TCGTCCTAAGGAAATCGTCGCAAATTGCAATAAGTGTAACGAATGGACACTGGAACTGCAGGGAACTGAAACA TGAAGCCGTGAGACACTTTCCCAGACCCTGGCTGCATGGCCTCGGTCAACACGATATCATTAGCCTCTGGGATCAG

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TCCCTGAAACCCTGTGTGAAACTGACACCCCTCTGCGTCACCCTCAACTGTACCAATGCCAATCTGATGAAGAGAT ACTCCACCCAAGTGGACCCCGATCTGGCTGACCAACTGATTCACCTCCACTATTTCGATTGCTTTGCCGATAGCGC AATCCATCCCATCGGCCAACACGGAATGGAGGATGAGGATAGGGAAGTGCTGAAATGGAAATTCGATAGCCATCTG TGAAACACTGGCCCCTCACCGAAGAGAAAATCAAAGCCATTTGGCCTAGCAACAAGGGAAGGCCTGGCAATTTCCC GCAGTCCAGGCCTGAGCCTACCGCACCCCCAGCCGAGAGCTTTAGATTCGGCATTAGCAAAAAGGCTAAGGGATGG TTTTACAGACACCATTACGATAGCCGACACCCTAAGGTCAGCTCCGAGGTCCACATTCCCCTCGGCATGATGACCG CTTGCCAAGGCGTCGGCGGACCCAGTCACAAAGCCAGGGTACTGGCAGAGGCTATATCCCAGGTGAACACGCTAA CATTCCTCCCATTGTGGCCAAAGAGATTGTGGCAAACTGTGACAAATGCCAGCTCAAGAGTGAGGCTATTCACGGA CAGGTGAACTGTAGCCCTTCCGAGGGAACAAGACAGACTAGGAAGAACAGACGTAGAAGGTGGCGTGCGAGGCAAA GGCAAATCCACTCCATCTCCGAGAGGATTCTGGGACAGATGAGGGAACCCAGAGGCTCCGACATTGCCGGTACTAC AAGCACACTGCAAGAGCAAATCGCATGGATGACAAGCAATCCCCCTAGCATTCAACAAGAGTTTGGCATTCCCTAT AACCCTCAGTCCCAGGCGTCGTGGAAAGCATGAACAAAGAGCTAAAGAAAATCATTGGCAGACAGGAGATCCTCG ATCTCTGGGTCTACCATACCCAAGGCTATTTCCCTGACTGCAGAATTACACACCCCGGACCCGGAGTCAGATACCC TAGCAGAGAAAGACAGAGACAGATTCATTCTATTAACGAATGGATTCTCAGCAACTGCCTCGGCAGATCCGCTGAG CCTGTGCCTCTGCAACTGTATAAGACACTGAGAGCCGAACAGGCTACCCAAGAGTCAAGAATTGGATGACCGAGA CACTGCTCGTGCAAAACGCTAACCCTGACTGTGAGAGAGTGTATCTGGCTTGGGTCCCCGCTCATAAAGGCATTGG CGGAAACGAACAGGTGGACAAACTGGTCAGCGCTGGCATTAGGAAAACAGACCCTAACCCTCAGGAAATCCATCTG TGAAATGCAATAACAAAAGGTTCAACGGAACTGGACCCAGTAAGAATGTGTCCACCGTCCAGTGTACCCATGGCCT AGAGCTCAAGAATAGCGCTATCTCCCTGCTCAACGCTACCGCTATCGCTGTGGCTGGGTGGACCGATAGGGTTATC GAAGTGGTTCAGTCCCGGCATCCCAAAGTGTCCAGCGAAGTGCATATCCCTCTGGGAGACGCTAGGCTCATCATTA GGACATACTGGGGCCTCCACACAGGGCGCTGCTATGGGCGGTAAATGGTCCAAGTGCTCCCTCGTCGGATGGCCCGC AGTGAGAGAGAATCAGACAGACACCCCCTGCCGCTGAGGGGGTGCTCAAGACCGGCAAGTACTCTAGGAAGAGG GGTGCCCATACCAATGACGTCAAGCAACTGACAGAGGCTGTGCAAAAGATTGCCACAGAGTCTAGCTGGGAGGGTC TGAAATACTGGGGGAATCTGCTCCAGTACTGGGGCCAGGAACTGAAAATCTCCGCCGTCAGCCTCCTGAATGCCAC AGCCATTGAGCTGCCTGAGAAAGAAGCTGGACCGTCAACGATATCCAAAAGCTCGTGGGAAAGCTCAACTGGGCA TCCCAGATTTACCCCGGAAGAGCCATTGAGGCTCAGCAACACATGCTGCAACTGACAGTGTGGGGCATTAAGCAAC TGCAAGCCAGAGTGCTCGCCATTGAGAGATACCTCGCCCTCCAGGATAGCGGATTGGAAGTGAATATCGTCACCGA TAGCCAATACGCTCTAGGCATCATTCAGGCTCAGCCTGACAAAAGCGAAAGGGAAATCTCCAACTATACCAATCAG ATTTACAAGATCCTCACCGAATCTCAAAAATCAACAGGATAGGAATGAGAAAGACCTCCTGGCTCCCACAAAGGCTA AGAGAAGGGTCGTGCAAAAGGGAAAAGCGTGCCGTCGGCATTGGCGCTATGTTTCTCGGATTCCTCGGCGCTGCCAA ACCCAAAATGATCGGAGGCATTGGAGGCTTTATCAAAGTCAGGCAGTATGACCAAATCCTTATCGAAATCTGTGGA AACAAGGCTATCTCCTACCATAGGCTCAGGGATTTCATTCTGATCGTCGCTAGGATTGTGGAACTGCTCGGCCGTA GCTCCCTGAAAGGCCTCCAGAGAGGCACACTGAATGCCTGGGTGAAAGTGATTGAGGAAAAGGGATTCAGTCCCGA AGTGATTCCCATGTTTTCCGCTCTGTCCGAGGGAGCCACACTCGAGtgaagatctgaattc

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B2 fragment

qqatccaccATGCTCGAGAATATGCTCACCCAAATCGGATGCACACTGAATTTCCCTATCTCCCCCATTGACACAG TGCCTGTGAAACTGAAACCCGGAATGGATGGCGCCGCCATCTTTAGGCCTGGCGGAGGCAATATGAAAGACAATTG GAGAAGCGAACTGTATAAGTATAAGGTCGTGAAGATTAAGCCTCTGGGAATCACATGGATTCCCGAATGGGAGTTC GTCAACACCCCCACTGGTCAAGCTATGGTATCAGCTGGAGAAAGAGCCTATCGTTGGCGCTGAGCCTCAGGATC CGCTGTCCTGTTTCTGGATGGCATTAACAAAGCTCAAGAGGAACATGAGAAGTATCACTCCAACTGGAGGACAATG GCCAACGACTTTAATCTGATGAAGCATCTCGTCTGGGCCTCTAGGGAGCTGGAGAGATTCGCTCTGAATCCCGGCC TGTCAAAACCATTATCGTCCACCTCAACGAAAGCGTCGAGATTAACATGGGCGCTAGGGCAAGTGTCCTCAGCGGC GGCAAGCTGGACGCCTGGGAAAAGATTAGGCTCAGGCCTGGCGGCAAGAAAAGTATAGGCTCAAGGAGAAGGGAG GCCTGGACGGACTGATTTACTCCCAAAAGAGGCAAGACATTCTGGATCTGTGGGTGTATAACACACAGGGATTCAC TAGATGGGGAACCTTGATCCTCGGCTTGGTGATTATCTGTAGCGCCAGCGAGAATCTGTGGGTGACAGTGTATTAC GGAGTGCCTGTGGGGGGGGGACAGCTCCTGTCCGGCATTGTGCAACAGCAAAATAACCTCCTGAGGGCTATCGAAG CCCAACAGCATCTGCTCCAGCTCACCGTCTGGGTCAGGCATTTCCCCAGGCCTTGGCTCCACAGCCTGGGACAGTA CATCTATGAGACATACGGAGACACATGGTCGGGAGTGGAAGCCCTCAAAAGCCCCAAAAAAGATTAAG CCTCCCCTCCCATCCGTGAAAAAGCTCACCGAAGACAAATGGAATAAGCCTCAAAAGACATATAGCGCTGGCGAAA GGATTGTCGATATCATTGCAACCGACATTCAGACTAAGGAACTGCAAAACCAAATCATAAAGATTCAGAATTTCGC TGTGTTTATCCATAACTTTAAGAGGAAGGGAGGCATTGGCGGCTACTCCGCCGGAGAGAAATCATTGACATTATC GCCAGCGATATCGTTCCCGTGGGCGATATCTATAAGAGATGGATCATTCTGGGACTCAACAAAATCGTGAGAATGT ATTCACCCGTCAGCATTCTGGATATCAGAGTGAGACAGGGATACTCCCCCCTCAGCTTTCAGACACTGATGCCCGC CCTCTGTCTCAGACAAGGGGAGACAATCCCACAGACCCTAAGGAAAGCAAAAAGGCTAGTGGAGTGGTCGAGTCCA TGAATAAGGAACTGAAAAAGATTATCGGACAGGTCAGGACCAGGCTGAGCACCTGAAAACCGCTGTGCAAATGGC CCCATTGCCCCTCTCACCGAGATTTGTAAAGAAATGGAAAAAGAAGGCAAAATCTCCAGGATTGGCCCTGAGAATC CCTATAACACCCCGTCTTTGCCATTCAAGTGAGAGACCAAGCCGAACACCTCAAGACAGCCGTCCAGATGGCAGT GACTTTAGGGAGCTCAACAAACGTACACAGGATTTCTGGGAGGTCCAGCTCGGCTTTTCGGCTCTGGCTTGGGATG ACCTCAGGAGCCTGTGTCTGTTCAGCTATCACAGACTGAGAGACTTTATCCTCATCGTTGCCAGAACCTGCCGACA TAGCAGAATCGGCATCACTAGGCAACGTAGAGGTAGGAACGGCTCCTCCAGGTCCGCTGCCCCCAAAATCTCCTTC GACCCCATTCCCATTCACTATTGCGCTCCCGCTGGCTTCGCTATCCTCAAGTGTAACAATAAGACATTCAATGGCG AAAAGGATTGGCATCTGGGACAGGGAGTGTCCATCGAATGGAGAAAGGAAAAGCTATAGCACACAGGTGGACCCTGA CCTCGCCGATCAGCCTAGCCTCTATCCTCCCTTAGCTTCCCTGAAAAGCCTCTTCGGAAACGATCCCTCATCCCAA GCCGCTAGAAGGGCTATCCTCGGCCAAATAGTCAGGAGAAGGTGTGAGTATCAGTCCGGACACAATAAGGTCGGCT CCCTGCAATACCTTGCACTCAGCCAACCCAAAACCGCTTGCTACAAGTGTTACTGTAAGAAATGTTGCTACCACTG TCAGGTCTGCTTCCTGAAGAAGGGACTGGGGAATCAGGGATTACGGAAAGCAAATCGCTGGCGCTGACTGTGGCCC AGCAGGCAAGACGCAAGCCCAAGTACCATAGCAATTGGAGAACCATGGCCAGTGAGTTTAACCTCCCCCCTA TCGTCGCTAAGGAAATCGTCGCAAGTTGTGATAAGTGTAACGAATGGACACTGGAACTGCTGGAGGAACTGAAACA TGAAGCCGTGAGACACTTTCCCAGACCCTGGCTGCATGGCCTCGGTCAACACGATATCATTAGCCTCTGGGATCAG

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TCCCTGAAACCCTGTGTGAAACTGACACCCCTCTGCGTCACCCTCAACTGTACCAATGCCAATCTGCTGAAGAGCT ACTCCACCCAAGTGGACCCCGATCTGGCTGACCATCTGATTCACCTCCACTATTTCGATTGCTTTTCCGATAGCGC AATCCATCCCATGGGCCTACACGGAATGGAGGATGAGGAAAGGGAAGTGCTGAAATGGAAATTCGATAGCCATCTG GCAGTCCAGGCCTGAGCCTACCGCACCCCCAGCCGAGAACTTTAGATTCGGCATTAGCAAAAAGGCTAAGGGATGG TTTTACAGACACCATTACGAAAGCCAACACCCTAAGGTCAGCTCCGAGGTCCACATTCCCCTCAGCATGATGACCG CTTGCCAAGGCGTCGGCGGACCCAGTCACAAAGCCAGGGTACTGGCAGAGGCTATGTCCCAGGTGAACACGCTAA CATTCCTCCCATTGTGCCCAAAGAGATTGTGGCAAACTGTGACAAATGCCAGCTCAAGGGTGAGGCTATGCACGGA CAGGTGGACTGTAGCCCTTCCGAGGGATCAAGACAGGCTAGGAAGAACAGACGTAGAAGGTGGCGTGAGAGGCAAA GGCAAATCCGCGCCATCTCCGAGTGGATTCTGGGACAGATAAGGGAACCCAGAGGCTCCGACATTGCCGGTACCAC AAGCACACTGCAAGAGCAAATCGCATGGATGACAAACAATCCCCCTGGCATTAAGCAAGAGTTTGGCATTCCCTAT AACCCTCAGTCCCAGGGCGTCGTGGAAAGCATGAACAAAGAGCTCAAGAAAATCATTGGCAGACAGGAGATCCTCG ATCTCTGGGTCTACAATACCCAAGGCTTTTTCCCTGACTGGCAGAATTACACACCCGGACCCGGAATCAGATACCC TAGCAGAGCAAGACAGACAGATTCATGCTATTAGCGAAAGGATTCTCAGCAACTTCCTCGGCAGACCCGCTGAG CCTGTGCCTCTGCAACTGTATAAGACACTGAGAGCCGAACAGGCTACCCAAGAGGTCAAGAATTGGATGACCGACA CACTGCTCGTGCAAAACGCAAACCCTGACTGTGAGAAAGTGTATCTGGCTTGGGTCCCCGCTCATAAAGGCATTGG CGGAAACGAACAGGTGGACAAACTGGTCAGCGCTGGCATTAGGAAAACAGACCCTAACCCTCAGGAAATCGATCTG TGAAATGCAATAACAAAAAGTTCAACGGAACTGGACCCTGTAAGAATGTGTCCACCGTCCAGTGTACCCATGGCCT AGAGCTCAAGAATAGCGCTGTCTCCCCTGCTCAACGCTACCGCTATCGCTGTGGCTGAGTGGACCGATAGGGTTATC GAAGTGGTTCAGTCCCAGCATCCCAAAGTGTCCAGCGAAGTGCATATCCCTCTGGGAGACGCTAGGCTCGTCATTA AGACATACTGGGGCCTCCACACAGGGGGTGCTATGGGCGGTAAATGGTCCAAGTGCTCCCTCGTCGGATGGCCCGC AGTGAGAGAGAATCAGACAGACACCCCCTGCCGCTGAGGGGAGTGCTCAAGACCGGCAAGTACTCCAGGATGAGG AGTGCCCATACCAATGACGTCAAGCAACTGACAGAGGTTGTGCAAAAGATTGCCACAGAGTCTAGCTGGGAGGGTC TGAAATACTTGTGGAATCTGCTCCTGTACTGGGGCCTGGAACTGAAAAACTCCGCCGTCAGCCTCCTGAATGCCAC AGCCATTGTGCTGCCTGAGAAAGGAAGGCTGGACCGTCAACGATATCCAAAAGCTCGTGGGAAAGCTCAACTGGGCA TCCCAGATTTACGCCGGAAGAGCCATTGAGGCTCAGCAACACTTGCTGCAACTGACAGTGTGGGGCATTAAGCAAC TGCAAGCCAGAGTGCTCGCCATTGAGAGATACCTCGCCCTCCAGGATAGCGGATCGGAAGTGAATATCGTCACCGA TAGCCAATACGCTCTAGGCATCATTCAGGCTCAGCCTGACAAAAGCGAAAGGGAAATCTCCAACTATACCAATCAG ATTTACAAGATCCTCACCGAATCTCAAAATCAACAGGATAGGAATGAGCAAGAACTCCTGGCTCCCACAAAGGCTA AGAGAAGGGTCGTGCAAAAGGGAAAAGCGTGCCGTCGGCATTGCGCGCTATGTTTTTCGGATTCCTCGGCGCTGCCAA ACCCAAAATGATCGGAGGCATTGGAGGCTTTATCAAAGTCAGGCAGTATGACCAAATCCTTATCGAAATCTGTGGA CAGAAGGCTATCTCCTACCATAGGCTCAGGGATTTCATTCTGATCGTCGCTAGGATTGTGGAACTGCTCGGCCATA GCTCCCTGAGAGGCCTCCGGAGAGGCACACTGAATGCCTGGGTGAAAGTGGTTGAGGAAAAGGGATTCAATCCCGA AGTGATTCCCATGTTTACCGCTCTGTCCGAGGGAGCCACACTCGAGtgaagatctgaattc

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qqatccaccATGCTCGAGAGCAACACCCCGCTAATAATGCCGATTGCGCGTGGCTGAAAGCCCAGGAAGAGGAAG AAGTGGGATTTCCTGTGAGACCCCAAGTGCCTAGAGCTTGGAGGGCTATCCTCAACATTCCCAGGAGGATTAGGCA AGGCTTTGAGAGAGCCCTCCTAGCCGCCGAATGGGACAGGGTTCACCCTGTGCACGCTGGCCCTGTCGCTCCCGGC CAAATGAGAGAGCCCAGAGGAAGCGATATCGCTGGCACAACCCTCAGGCCCATGACATATAAGGCCGCTATTGACC TCAGCTTGTTTCTGAAAGAGAAAGGCGGACTGGAAGGCCTCATCTATAGCAAGAAAGCTGCTATGGAACAGGCTCC CAAGGCCAATGGACCTACCAAATCTTTCAGGAACCCTTTAAGAATCTGAAAACCGGAAAGTATTCCAGAATGAGAA GCGCTCACACAAACTGGATGACAGAAACCCTCCTGGTCCAGAATGCCAATCCCGATTGCAAGTCCATCCTCAGGGC TCTGGGAACCGGAGCCACACTGGAAGAGCCTGAGGTCATCCCTATGTTCTCAGCCCTCAGCGAAGGCGCTACCCCC CAAGACCTGAATACGATGCTCAACATCGTCAGCGGACACCCAATCCACCCTCCAGGAACAGATTGGCTGGATGACAA ATAACCCTCCCATCCCTGTCGGAGAGATTTACAAAAGGTGGATTATCCTCGGCCTGACTAGAATCCCCCATCCCGC CGGCCTCAAGAAAAAGAAAAGCGTCACCGTCCTGGATGTGGGAGACGCTTACTTCAGCGTCCCCCTCGACGAAGAC CAAAAGGAAACCTGGGAGGCTTGGTGGACGGAATACTGGCAGGCTACCTGGATTCCTGAGTGGGAGTTTGTGAATA CCCCTCCCTCGTGTTTCCCGATTGGCATAACTATACCCCTGGCCCTGGCATAAGGTATCCCCTCACCTTTGGATG GTGCTTTAAGCTCGTGCCTGTGGACCCCAAACTGTGGTACCAACTGGAAAAGGAACCCATTGTCGGAGCCGAAACC TTTTACGTGGACGGAGCCGCCAACAGAGAGACAAAGCTCGGCCAAAACGTCCAGGGACAGATGGTGCATCAGGCTA TTAGCCCCAGGACCCTCAACGCTTGGGTCAAGGTCGTCGAAGAGAAAGCCTTTAACGAAACCGAAGTGCATAACGT CTGGGCTACCCATGCCTGTGTGCGTACCGATCCCCAATCCCCAAGAGATTCTCCTGGAGAATGTGACAGAGCTCAAG GATCAGAAACTCCTCGGCATTTGGGGATGCTCCGGCAAAATCATTTGCACAACCACTGTGCCTTGGAACAGCTCCT GGTCCAACCAAGCTGGCCATAACAAAGTGGGAAGCCTCCAGTATCTGGCTCTGACGGCTCTGATTAAGCCTAAGAA AATCAAACCCCCTCTGCCTAGCGTTAAGACAATCATTGTGCATCTGAATGAGTCCGTGGAAATCAATTGCACAAGG CCTAACAATAACACAAGGAAAGCCGCCGCTAGTGAAGTACGGAATAAGTCCAAACAGAAAACCCAGCAAGCTGCCG CCGATACAGGCGACTCCAGCCAGGTCAGCCAAAACTATCCCATTGTGTCCAACTTTACCTCCACCACTGTGAAAGC CGCTTGTTGGTGGGCCAATATCAAACAGGAGTTTGGAATCCCTTACAATCCCCAAAGCCAAACATTCTATGTGGAT GAATCTGGCAGCTCGACTGTACCCATCTGGAAGGCAAAGTCATTCTGGTAGCCGTCCACGTCGCCTCCGGCTACAT TGAGGCTGAGGTCGGCAATGAGCAAGTGGATAAGCTCGTGAGTTCCGGAATCAGAAAGGTGCTATTCCTCGACGGA ATCAATAAGGCTCAGGAAGAGCACGAAGTCAGGGAAAGGATTAGGCGAACCGCTCCCGCTGCTGAAGGCGTCGGCG CTGTCTCCCAGGATCTGGATAAGTACGGAGCCCTCACCTCCACAGCGGAACCCAACAGTCCCAGGGAACTGAAAC TGGCGTCGGCAACCCTCAGATTTTGGGAGAGTCCAGCGTTGTCCTCGGCTCCGGCTCCATCGTCATCTGGGGTAAA ACCCCTAAGTTTAAGTTCCCCATTCAGAAAGAGACATGGGAAGCCTGGTGGACGGAGTATTGGCAAGCCGCTGCTT ACAGACTGATCAGCTGTAACACAAGCGTTATCAAACAGGCTTGCCCTAAGATTACCTTTGACCCTATCCCTATCCA TTACTGTGCCCCTCCTAGCTGGATGGGCTATGAGCTCCACCCTGACAGATGGACAGTGCAACCCATCGTGCTCCCC GAAAAGGACTCCTGGACAGTGAATGACATTCAGAAATCAATTCTGAGAGCCCTCGGCCCAGGCGCTTCCCTGGAGG AAATGATGACAGCATGTCAGGGAGTGGGAGGCCCTGGCCATAAGGCTAGAGTGTATTACAGAGACTCCAGGGACCC CATTTGGAAAGGCCCTGCCAAACTGCTCTGGAAAGGCGAAGGCGCTGTGGTCATCCAAGACATTAAGATTGGAGGC CAACTGATAGAAGCCCTCCTGGATACAGGAGCCGATGACACCGTCCTGGAAGATATGAATCTGCCTGGCAAGTGGG GAATCAAACAGCTCCAGGCTAGGGTCCTGGCTATCGAGAGGTATCTGAAAGATCAACAGTTTCTGGGACTCTGGGG CTGTAGCGGAAAGGCTGCTATGGAAAACAGATGGCAAGTGATGATCGTCTGGCAAGTGGACAGGATGAAGATTAGG

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ACATGGAATAGCCTCGTGAAACACCATATGTATATTATCTGTACCACAACCGTCCCCTGGAACTCCACCTGGAGCA ATAAGTCCTTCGAAGAGTTTGGAATAACATGACCTGGATTCAATGGCTGATTCTCGCTATCGTCGTGTGGACCAT TGTGTATATCGAATACAAGAAACTGCTCAGGCAAAGGAGAATCGATAGGCTCATCAAAAGGCTCAACCCTGGCCTC CAATGAGTCCGAGGGAGACACACCCGGAATCAGATACCAATACAATGTGCTCCCCCAAGGCTGGAAGGGCTCCCCA CCCATTTCCAAAGCTCCATGACCCAAATCCTCATGATGCAAAGGGGAAACTTTAAGGGACAGAAAAGGATTATCA AGTGCTTCAACTGTGGAAAGGAAGGCCATCTCGCTAGGAATTGCAGACCTCCCCTAGAGAGACTGAACCTGGATTG CTCCGAGGATAGCGACACCTCCGGCACACAGCAAAGCCAAGGCACAGAGACAGAAGTGGGACTCGTGGCTGTGCAT GTGGCCAGCGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTATCCTCAAGA TTAAGCCTGTGGTCAGCACAGCTCCTGCTCAACGGTAGCCTCGCTGAAGAGGGAAATCATTATCAGAAGCGAAAA CTTTACCGATAACAAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACGCTGGCATCAAAGTGAAGCAACTG ATGTGAATGCTGCTCAAACCAGAGGCGATAACCCTACCGGTCCCGAAGAGTCCAAGAAGAGGTCGCGTCCAAGAC AGAGACAGACCCTTGTGACGCCCCCTAGCTCCAACTTTCTGGGAAGGTCTGCCGAACCCGTCCCCTCCAGCCC GGTTCAATATCACCAACTGGCTGTGGTACATTAAGATTTTCATTATGATTGTGGGAGGCAATAAGATTGTCAGGAT GTACTCACCTGTCTCCATCCTCGACATTAAGCAAGGCCCTAAGGAACCCTTCAGGGATTACGTGGACAGATTCGCT AAGCTCCTGTGGAAGGGAGAGGGAGCCGTCGTGATTCAGGACAACTCCGACATTAAGGTCGTGCCCAGGAGAAAGG ${\tt CTAAGATTATCGAACTGAATAAGAGAACCCAAGACTTTTGTGAAGTGCAACTGGGAATCCCTCACCCTGCTGGACT}$ GAAGAAAAAAGTCAGTGACAGTGGCCGCTATGAGAGTGAAAGAGACACAGATGAACTGGCCCAATCTGTGGAAG TGGGGCACAATGATTCTGGGACTGGTCATCATTTGCTCCGCCTCCATTAAGGTCAGACAGCTCTGCAAACTGCTCA GGGGTACAAAGGCTCTGACAGAGATTGTGACACTGACAGAGGAAGCCGAACTGCACATATGGAAGTTTGA CTCCCGCCTCGCCCTGAGACATATCGCCAGGGAACTGCATCCCGAGTTCTACAAAGACTGCGCTGCTGTCGAGCTC CTGGGACGCTCCAGCCTCAAGGGACTGCAAAGGGGATGGGAAGGCCTCAAGTATTTGTGGAACCTCCTGCAGTATT GGGGCTCTAGCCTGGGGCAACTGCAACCTGCTCTGAAAACCGGATCAGAGGAACTGAAGTCCCTGTATAACACAAT CGCTACCCTCTGGTGTGTGCATCAGGAGCTCTACAAATACAAAGTGGTCAAAATCAAACCCCTCGGCATTGCCCCT ACCAGAGCCAAAAGGAGGGGTGGTCGAGAGAGAGAAAAGGCTCACCGAAATCGTCCCACTCACCGAAGAGGCTGAGC TGGAGCTGGAGGAAAACAGAGAGATTCTGAGGGAACCCGTCCACGGAGTGTATAGAGTGCTCGCCGAAGCCATGAG CCAAGTCAACAATGCCAACATCATGATGCAGAGGGCAATTTCAAAGGCCTAAAGAGAATCATCAAACAAGAGGAA GAGGAGGTCGGCTTCCCCGTCAGGCCCCAGGTCCCACTGAGACCTATGACCTACAAAGGAGCCGTCGATCTGTCCT TCTTCAGACAGGGACCCAAAGAGCCTTTCAGAGACTATGTGGATAGGTTTTTCAAAACCCTCAGGGCTGAGCAAGC CTCACAGGAAGTGAAAAACTGGGAGAAAATCAGACTGAGACCTGGTGGCAAAAAGAAATACAAAATGAAACACATT GTGTGGGCCTCCAGGGAACTGGAAAGGTTTGCCTCCCAGTATGCCCTCGGCATCATCCTAGCCCAACCCGATAAGT CCGAGTCCGAGCTCGTGAATCAGATTATCGAAGAGCTCATCAAGAAGATTGCCGTCGCCGGATGGACAGAAT GGGCTGATGTGAAACAGCTCACCGCAGTCGTCCAGAAAATCGCTACCGAAAGCATTGTGATATGGGGAAAGACGCC CAAGTTCAGACTGCCTATCGCTGCCGCCAGCAACGAGAACATGGAGACCATGGCTGCTtgaagatctgaattc

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C2 fragment

ggatccaccATGCTCGAGAGCAACACAGCCGCTAACAATACCGATTGCGTGTGGCTGAAAGCCCAGGAAGAGAGAAGA AAGTGGGATTTCCTGTGAGACCCCAAGTGCCTAGAGCCGGGAGGGCTATCCTCAACATTCCCACGAGGATTAGGCA AGGCCTTGAGAGAGCCCTCCTAGCCGCAGATGGGATAGGATTCACCCTGTGCACGCTGGCCCTATCGCTCCCGGC CAAATGAGAGAGCCCAGGGGAAGCGATATCGCTGGCACAACCCTCAGGCCCATGACATATAAGGCCGCTATTGACC TCAGCTTGTTTCTGAAAGAGAAAGGCGGACTGGATGGCCTCATCTATAGCAAGAAAGCTGCTATGGAACAGGCTCC CGAAGACCAAAGCTCTCAGAGAGAGCCTTACAATGAGTGGACCCTGGAGGCTCCTGGAAGAGCTCAAGCACGAGGCT CAAGGCCAATGGACCTTCCAAATCTTTCAGGAACCCTTTAAGAATCTGAAAACCGGAAAGTATGCCAGAATGAGAG GCGCTCACACAACTGGATGACAGATACCCTCCTGGTCCAGAATGCCAATCCCGATTGCAAGTCCATCCTCAAGGC TCTGGGACCCGGAGCCTCACTGGAAGAGCCTGAGGTCATCCCTATGTTCTCAGCCCTCAGCGAAGGCGCTACCCCC CAAGACCTGAATATGATGCTCAACACCGTCGGCGGACACCAATCCACCCTCCAGGAACAGATTGGCTGGATGACAA ATAACCCTCCCATCCCTGTCGGAGAGATTTACAAAAGGTGGATTATCCTCGGCCTGACTAGAATCCCCCATCCCGC CGGCCTCAAGAAAAAGAAAAGCGTCACCGTCCTGGATGTGGGAGACGCTTACTTCAGCGTCCCCCTCGACGAAGGC CAAAGGGAAACCTGGGAGGCTTGGTGGATGGAATACTGGCAGGCTACCTGGATTCCTGAGGGGGAGTTTGTGAATA CCCCTCCCTCGTGTTTCCCGATTGGCAAAACTATACCCCTGGCCCTGGCACAAGGTATCCCCTCACCTTTGGATG GTGCTTTAAGCTCGTGCCTGTGGACCCCAAACTGTGGTACCAACTGGAAAAGGACCCCATTGTCGGAGTCGAAACC TTTTACGCGGACGGAGCCGCCAACAGAGAGACAAAGCTCGGCCAAAACGTCCAGGGACAGATGGTGCATCAGCCTA TTAGCCCCAGGACCCTCAACGCTTGGGTCAACGTCATCGAAGAGAAAGGCTTTAGCGACACCGAAGTGCATAACGT CTGGGCTACCCATGCCTGTGTGCCTACCGATCCCAATCCCCAAGAGATTCTCCTGGAGAATGTGACAGAGCTCAAG GATCAGAAACTCCTCGGCATTTGGGGATGCTCCGGCAAACTCATTTGCACAACCACTGTGCCTTGGAACAGCTCCT GGTCCAACCCAGCTGGCCATAACAAAGTGGGAAGCCTCCAGTATCTGGCTCTGAAGGCTCTGATTACGCCTAAGAA AATCAAACCCCCTCTGCCTAGCGTTAAGACAATCATTGTGCATCTGAATGAGTCCGTGGAAATCAATTGCACAAGG CCGATACAGGCAGCTCCAGCAAGGTCAGCCAAAACTATCCCATTGTGTCCAACTTTACCTCCACCACTGTGAAAGC CGCTTGTTGGTGGGCCAATATCAAACAGGAGTTTGGAATCCCTTACAATCCCCAAAGCCGAACATTCTATGTGGAT GAATCTGGCAGCTCGACTGTACCCATCTGAAAGGCAAAGTCATTCTGGTAGCCGTCCACGTCGCCTCCGGCTACAT TGAGGCTGAGGTCGGCAATGAGCAAGTGGATAAGCTCGTGATTTCCGGAATCAGAAAGGTGCTATTCCTCGACGGA ATCGATAAGGCTCAGGAAGAGCACGAAGTCAGGGAAAGGATTAGGCGAGCCGCTCCCGCTGCTGAAGGCGTCGGCG CTGTCTCCCAGGATCTGGATAAGTACGGAGCCATCACCTCCACAAGCGGAACCCAACAGTCCCAGGGAACTGAAAC TGGCGTCGGCAACCCTCAGATTTTGGGAGAGTCCAGCGCTGTCCTCGGCTCCACCGTCATCTGGGGTAAA ACAGACTGATCAGCTGTAACACAAGCGTTATCACACAGGCTTGCCCTAAGATTAGCTTTGAGCCTATCCCTATCCA TTACTGTGCCCCTCGTAGCTGGATGGGCTATGAGCTCCACCCTGACAGATGGACAGTGCAACCCATCGTGCTCCCC GAAAAGGAGTCCTGGACAGTGAATGACATTCAGAAAACAATTCTGAAAGCCCTCGGCCCAGGCGCTACCCTGGAGG AAAATATGACAGCATGTCAGGGAGTGGGAGGCCCTGGCCATAAGGCTAGAGTGTATTACAGAGACTCCAGGGACCC CATTTGGAAAGGCCCTGCCAAACTGCTCTGGAAAGGCGAAGGCGCTGTGGTCATCCAAGACATTAAGATTGGAGGC CAACTGAAAGAAGCCCTCCTGGATACAGGAGCCGATGACACCGTCCTGGAAGATATCAATCTGCCTGGCAAGTGGG GAATCAAACAGCTCCAGGCTAGGGTCCTGGCTATCGAGAGGTATCTGAAAGATCAACAGCTTCTGGGAATCTGGAG CTGTAGCGGAAAGGCTGCTATGGAAAACAGATGGCAAGTGATGATCGTCTGGCAAGTGGACAGGATGAAGATTAGG

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ACATGGAATAGCCTCGTGAAACACCATATGTATCTTATCTGTACCACAGCCGTCCCCTGGAACTCCACCTGGAGCA ATAAGTCCTTCGAAGAGATTTGGAATAACATGACCTGGATTGAATGGCTGATTATCGCTATCGTCGTGTGGACCAT TGTGTTTATCGAATACAAGAAACTGCTCAGGCAAAGGAAAATCGATAGGCTCATCGAAAGGCTCAACCCTGGCCTC CAATGAGTCCGAGGGAGACACCCGGAATCAGATACCAATACAATGTGCTCCCCCAAGGCTGGAAGGGCTCCCCA GCCATTTTCCAAAGCTCCATGACCAAAATCCTCATGATGCAAAGGGGAAACTTTAAGGGACAGAAAAGGATTATCA AGTGCTTCAACTGTGGAAAGGAAGGCCATCTCGCTAGGAATTGCAGACCTCCCCTGGAGAGACTGAACCTGGATTG CTCCGAGGATAGCGACACCTCCGGCACACAGCAAAGCCAAGGCACAGAGACAGGAGTGGGACTCGTGGCTGTGCAT GTGGCCAGCGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTCTCCTCAAGA TTAAGCCTGTGGTCAGCACACGCTCCTGCTCAACGGTAGCCTCGCTGAAGAGGGAAATCATTATCAGAAGCGAAAA CTTTACCAATAACAAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACCCTGGCATCAAAGTGAGGCAACTG AGAGACAGACCCTTTTGACGCCGCCCCTAGCTCCACCTTTCTGGGAAGGTCTGTCGAACCCGTCCCCCTCCAGCTC ${\tt CCCCTCTGGAAAGGCTCCACCTCGACTGTAGCGAAGACAGTGACGAACTGGATAAGTGGGCCTCCCTGTGGAACT}$ GGTTCAATATCACCAACTGGCTGTGGTACATTAAGATTTTCATTATGATTGTGGGAGGCAATAAGATTGTCAGGAT GTACCAACCTGTCTCCATCCTCGACATTAAGCAAGGCCCTAAGGAACCCTTCAGGGATTACGTGGACAGATTCGCT AAGCTCCTGTGGAAGGGAGAGGGAGCCGTCGTGATTCAGGACAACTCCGACATTAAGGTCGTGCCCAGGAGAAAGG CTAAGATTATCGAACTGAATAAGAGAACCCAAGACTTTTGGGAAGCGCAACTGGGAATCCCTCACCATGCTGGACT GAAAAAGAAAAAGTCCGTGACAGTGGCCGCTATGAGAGTGAAAGAGACACAGATGAACTGGCCCAATCTGTGGAAG TGGGGCACAATGATTCTGGGACTGGTCATCATTTGCTCCGCCTCCATTAAGGTCAAACAGCTCTGCAAACTGCTCA GGGGTGCAAAGGCTCTGATAGACATTGTGCCACTGACAGAGGAAGCCGAACTGGAACTGCTCATATGGAAGTTTGA CTCCCACCTCGCCCTGAGACATATCGCCAGGGAACTGCATCCCGAGTACTACAAAGACTGCGCTGCTGTCGAGCTC $\tt CTGGGACGCTCCAGGCACTGCGAAGGGGATGGGAAGCCCTCAAGTATTTGTGGAACCTCCTGCAGTATT$ GGGGCTCTAGCCTGGAGCAACTGCAATCTGCTCTGAAAACCGGATCAGAGGAACTGAGGTCCCTGTTTAACACAGT CGCTACCCTCTGGTGTGCGCATCAGGAGCTCTACAAATACAAAGTGGTCAAAATCGAACCCCTCGGCATTGCCCCT ACCAAAGCCAAAAGGAGAGTGGTCCAGAGAGAGAAAAGGCTCACCGATATCGTCACACTCACCGAAGAGGCTGAGC TGGAGCTGGAGGAAAACAGAGAGATTCTGAAGGAACCCGTCCACGGAGTGTATAGAGTGCTCGCCGAAGCCATGAG CCAAGCCAACAATGCCAACATGATGCAGAGAGGGCAATTTCAGAGGCCCAAAGAGAATCATCAAACAAGAGGAA GAGGGGGTCGGCTTCCCCGTCAGGCCTCAGGTCCCACTGAGACCTATGACCTACAAAGCAGCCATCGATCTGTCCT TCTTCAAACAGGGACCCAAAGAGCCTTTCAGAGACTATGTGGATAGGTTTTTCAAAACCCTCAGGGCTGAGCAAGC CTCACAGGAAGTGAAAAACTGGGAGAAAATCAGACTGAGATCTGGTGGCAAAAAGAAATACAAACTGAAACACATT GTGTGGGCCTCCAGGGAACTGGAAAGGTTTGCCTCCCAGTATGCCCTCGGCATCATCCTAGCCCAACCCGATAAGT GGGCTGATGTGAAACAGCTCACCGAAGTCGTTCAGAAAATCGCTACCGAAAGCATTGTGATATGGGGAAAGACACC CAAGTTCAGACAGCCTATCGCTGCCGCCAGCAACGAGAACATGGACGCCATGGCTGCTtqaaqatctgaattc

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU01/00622 CLASSIFICATION OF SUBJECT MATTER Int. Cl. 7: C07K 19/00; C12Q 1/68; C07K 2/00, 14/005, 14/15, 14/20, 14/435; C12N 15/09 According to International Patent Classification (IPC) or to both national classification and IPC FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) SEE ELECTRONIC DATABASES BELOW Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched SEE ELECTORNIC DATABASES BELOW Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) CA WPIDS MEDLINE: Combinatorial protein/peptide/polypeptide; gene/DNA shuffling; domain swapping; vaccine; synthetic protein/peptide polypeptide DOCUMENTS CONSIDERED TO BE RELEVANT C. Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. Category* WO 00/18906 A. MAXYGEN INC. 6/4/00 All X All WO 99/41402 A. MAXYGEN INC. 19/8/99 Х All WO 99/41369 A. MAXYGEN INC. 19/8/99 X WO 99/41368 A. MAXYGEN INC. 19/8/99 All X All Ryu DDY and Nam D-H. Recent progress in biotechnological engineering. X. Biotechnol Prog. Jan-Feb 2000. 16: 2-16. All X Punnonen J. Molecular breeding of allergy vaccines and antiallergic cytokines. Int Arch Allergy Immunol. March 2000. 121: 173-182 See patent family annex Further documents are listed in the continuation of Box C later document published after the international filing date or priority date and not in conflict with the application but cited to "A" understand the principle or theory underlying the invention document of particular relevance; the claimed invention cannot "E" be considered novel or cannot be considered to involve an inventive step when the document is taken alone "L" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such "O" combination being obvious to a person skilled in the art document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search Authorized officer Name and mailing address of the ISA/AU **AUSTRALIAN PATENT OFFICE** PO BOX 200, WODEN ACT 2606, AUSTRALIA Gillian Allen E-mail address: pct@ipaustralia.gov.au

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INTERNATIONAL SEARCH REPORT

International application No.

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